



JUEVES, 23 OCTUBRE 2025

## Hepatocellular Carcinoma and Liver Transplantation from Milan criteria to personalized indications



UNIVERSITÀ  
DEGLI STUDI  
DI MILANO

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FONDAZIONE IRCCS  
ISTITUTO NAZIONALE  
DEI TUMORI

*(I have no conflict of interest in the contest of the subject of this presentation)*

# limits, barriers and borders

the limits to capital and the limits to nature, marxism and feminism, environment, nature and technologies, the politics of identity, the conceptualising marxist theories of racism, latin america and marxism(s), marxism, sexuality and political economy, 10-13 november, 2016, school of oriental and african studies, 10 thornhaugh street, russell square london wc1n 1dz  
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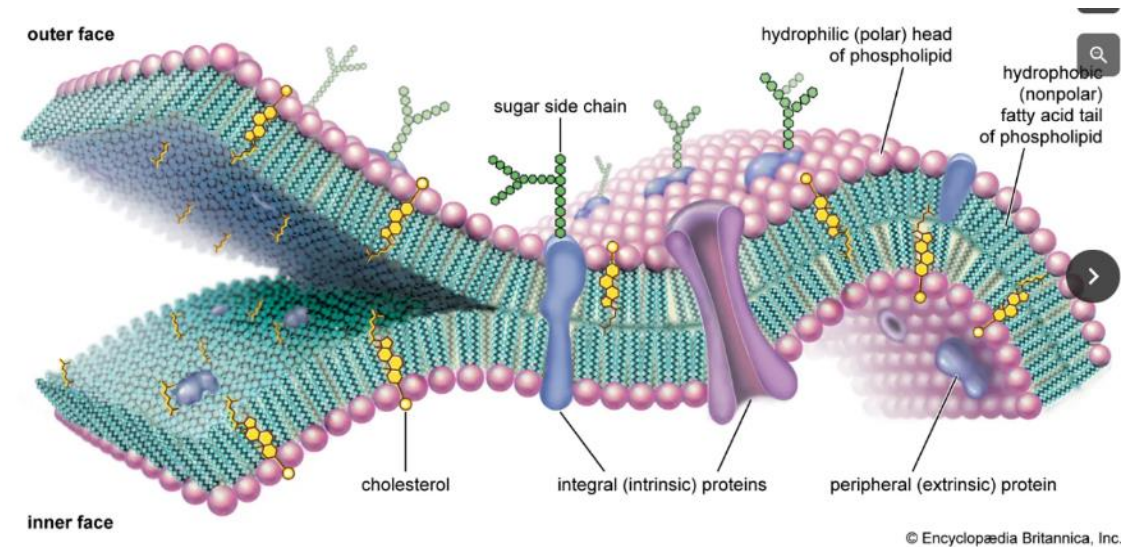
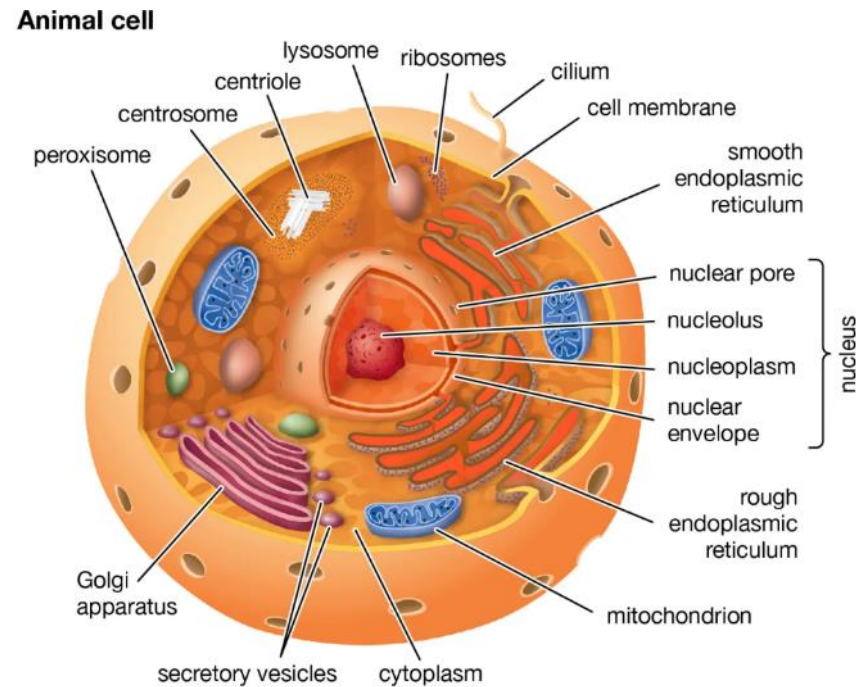
2016 annual conference





Complex living systems are thought to exist at the “edge of chaos” separating the ordered dynamics of robust function from the disordered dynamics of rapid environmental adaptation.

**Boundaries are an essential part of life  
since life only exists on the edge of chaos**



Bringing order and organization to the chaos depends on membrane-bound compartments

# The new era of Liver Transplantation for hepatic malignancies

## Article

### Gene-modified pig-to-human liver xenotransplantation

<https://doi.org/10.1038/s41586-025-08799-1>

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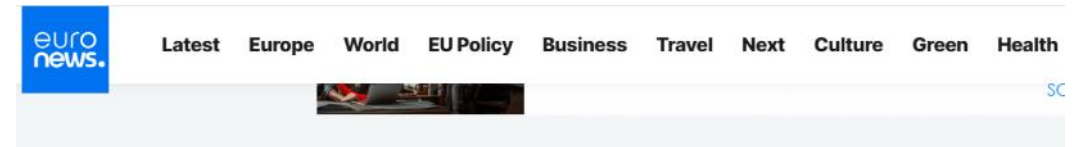
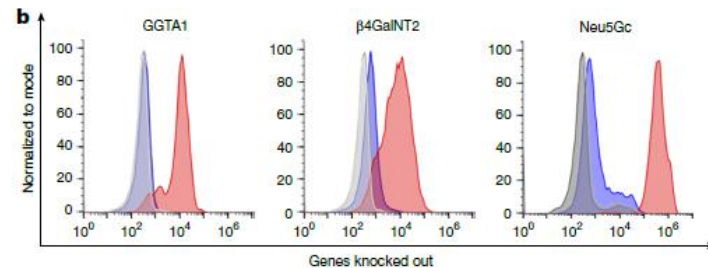
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Kai-Shan Tao<sup>1,16</sup>, Zhao-Xu Yang<sup>1,16</sup>, Xuan Zhang<sup>1,16</sup>, Hong-Tao Zhang<sup>1,16</sup>, Shu-Qiang Yue<sup>1</sup>, Yan-Ling Yang<sup>1</sup>, Wen-Jie Song<sup>1</sup>, De-Sheng Wang<sup>1</sup>, Zheng-Cai Liu<sup>1</sup>, Hai-Min Li<sup>1</sup>, Yong Chen<sup>1</sup>, Rui Ding<sup>1</sup>, Shi-Ren Sun<sup>2</sup>, Ming Yu<sup>3</sup>, Ji-Peng Li<sup>4</sup>, Wei-Xun Duan<sup>5</sup>, Zhe Wang<sup>6</sup>, Jing-Wen Wang<sup>7</sup>, Jia-Yun Liu<sup>8</sup>, Min-Wen Zheng<sup>9</sup>, Xi-Jing Zhang<sup>10,11</sup>, Wen Yin<sup>12</sup>, Wei-Jun Qin<sup>13</sup>, Dong-Mei Bian<sup>14</sup>, Lin Li<sup>1</sup>, Min Li<sup>1</sup>, Zhi-Bin Lin<sup>1</sup>, Hao Xu<sup>1</sup>, Dan Wei<sup>1</sup>, Hong Zhang<sup>1</sup>, Juan-Li Duan<sup>1</sup>, Deng-Ke Pan<sup>15</sup>, Hai-Long Dong<sup>11,16</sup>, Lin Wang<sup>11,16</sup> & Ke-Feng Dou<sup>11,16</sup>

The shortage of donors is a major challenge for transplantation; however, organs from genetically modified pigs can serve as ideal supplements<sup>1,2</sup>. Until now, porcine hearts and kidneys have been successively transplanted into humans<sup>3–7</sup>. In this study, heterotopic auxiliary transplantation was used to donate a six-gene-edited pig liver to a brain-dead recipient. The graft function, haemodynamics, and immune and



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### World's first pig-to-human liver transplant keeps patient alive for 171 days



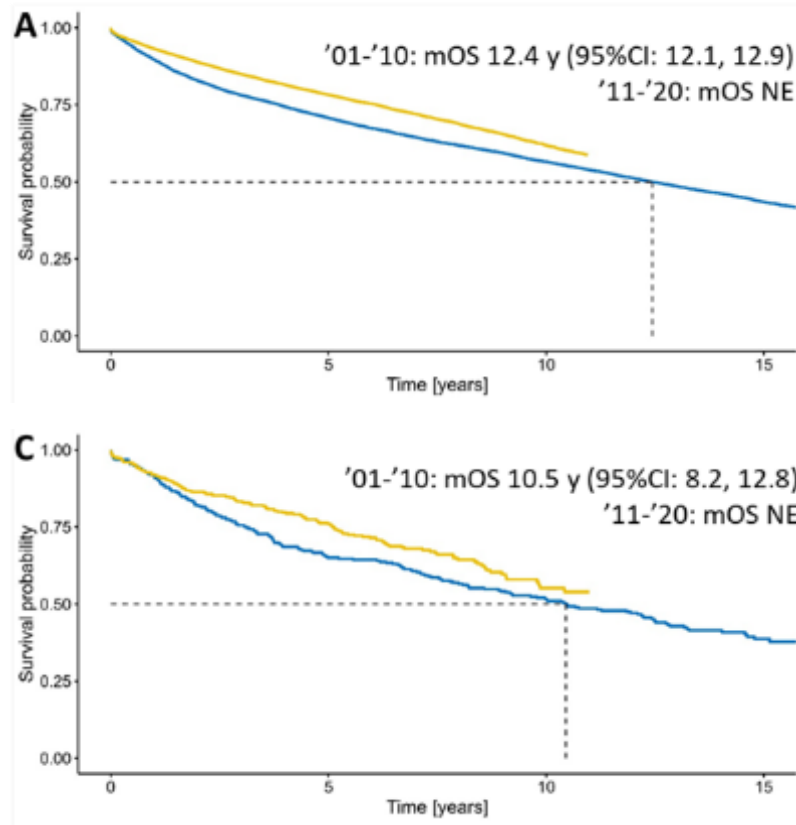
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By [Theo Farrant](#)

Published on 09/10/2025 - 6:02 GMT+2 • Updated 9:34

Despite strong learning attitude and open disposition to science liver transplantation for cancer remains a procedure at high cost, **limited in competitiveness by the distance between incidence of liver cancers and availability of donated organs**

# The new era of Liver Transplantation for hepatic malignancies

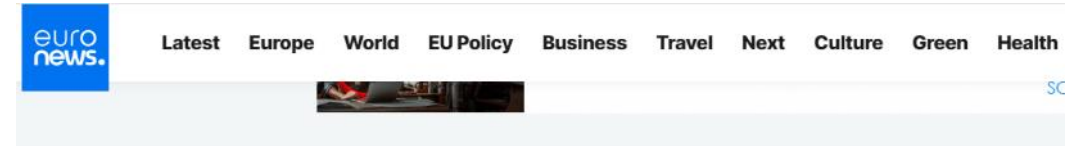


deceased donor  
**within Milan criteria**

deceased donor  
**beyond Milan criteria**

Pre-transplant therapies in this cohort include ablation (42%), TACE (30%), TARE (3%), resection (0.7%) and SBRT (0.6%)

Magyar CTJ et al. J Clin Oncol 2025



Health > Health news

## World's first pig-to-human liver transplant keeps patient alive for 171 days



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Published on 09/10/2025 - 6:02 GMT+2 • Updated 9:34

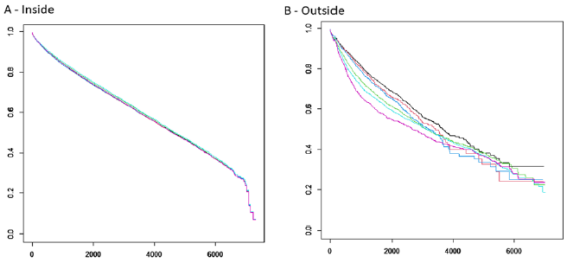
Despite strong learning attitude and open disposition to science liver transplantation for cancer remains a procedure at high cost, **limited in competitiveness by the distance between incidence of liver cancers and availability of donated organs**



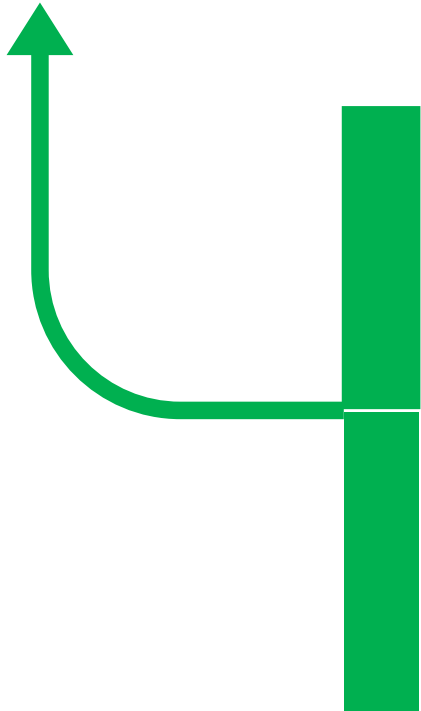
# Time to Expand Selection Criteria for MELD Exception Points in Liver Transplantation for Hepatocellular Carcinoma

Chase J. Wehrle, MD,<sup>1</sup> Jiro Kusakabe, MD, PhD, MPH,<sup>2</sup> Toshihiro Nakayama, MD,<sup>3</sup> Charles Miller, MD,<sup>1</sup> Koji Hashimoto, MD, PhD,<sup>1</sup> Timothy M. Pawlik, MD, PhD, MPH,<sup>4</sup> Kazunari Sasaki, MD, PhD,<sup>3</sup> Vincenzo Mazzaferro, MD, PhD,<sup>5</sup> Andrea Schlegel, MD, MPH,<sup>1</sup> and Federico Aucejo, MD<sup>1</sup>

National Cohort, Overall Survival



Wehrle CJ et al. Transplantation 2025



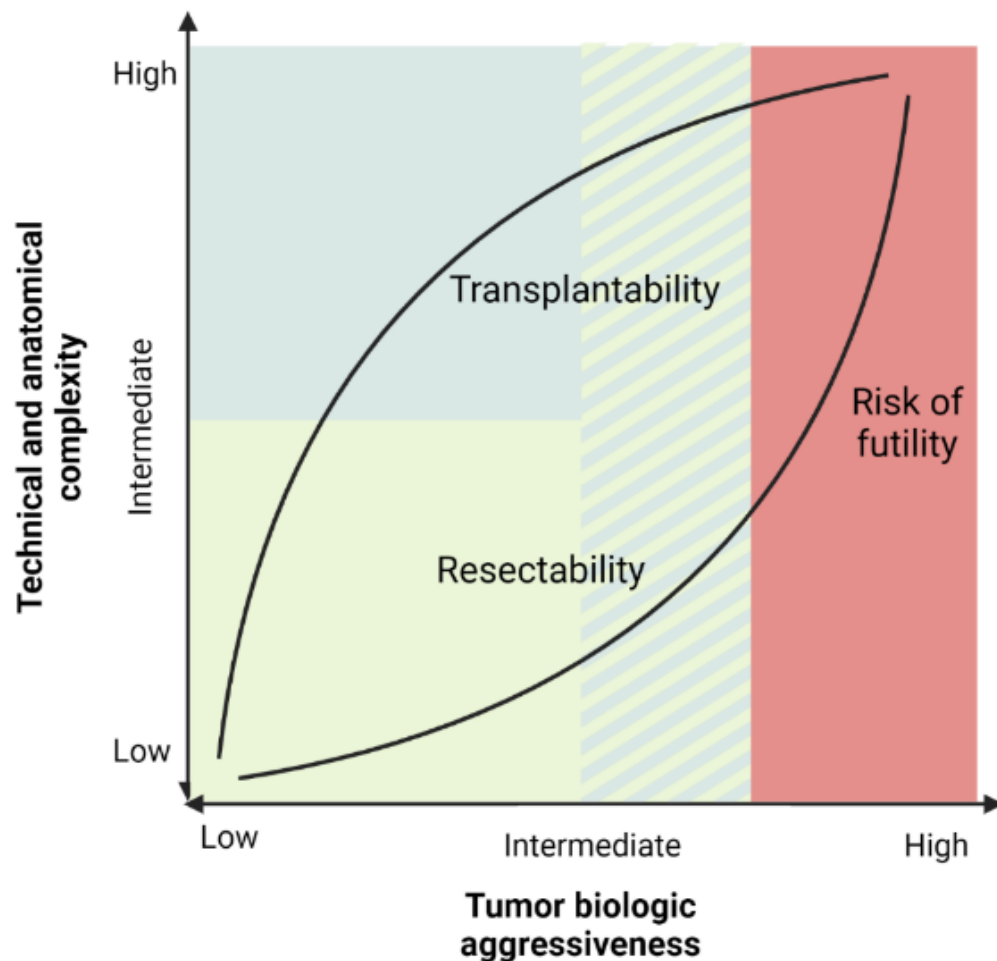
Transplantation ■ March 2021 ■ Volume 105 ■ Number 3

www.transplantjournal.com

TABLE 1.

## Consensus recommendations for the expansion of liver transplant indications in Spain

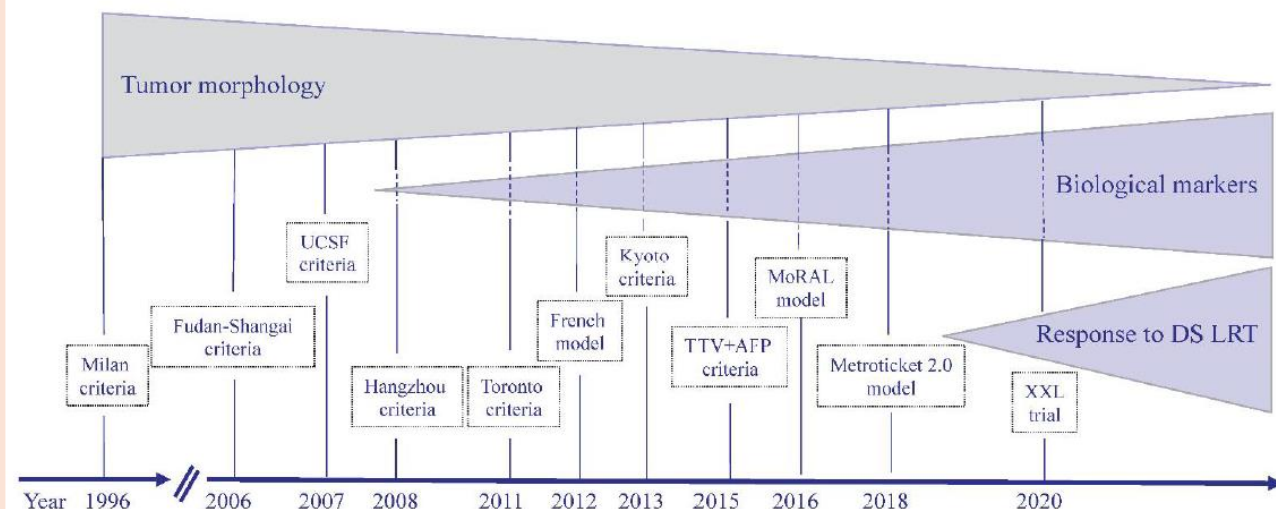
Recommendations		GRADE	Ref.
<b>2. Hepatocellular carcinoma</b>			
2.1	The presence of extrahepatic metastases or macrovascular invasion should preclude LT in patients with cirrhosis and hepatocellular carcinoma.	1A	18-22
2.2	Milan criteria are considered the standard of care to select candidates with hepatocellular carcinoma for LT.	1A	7,23
2.3	Patients within Milan criteria showing AFP >1000 ng/mL should undergo locoregional therapy to ensure a decline of AFP below 500 ng/mL to be included in the waiting list. If AFP remains >500 ng/mL, LT should be discouraged.	2C	24
2.4	A moderate expansion of Milan criteria is advised as long as the balance with other indications of LT is preserved.	1B	25,26
2.5	Among the expanded criteria for LT, the “Up-to-7” criteria are those with the strongest scientific background and may be preferred over other systems.	2B	27,28
2.6a	Patients beyond Milan but within “Up-to-7” criteria with serum AFP >400 ng/mL should undergo <u>locoregional therapy</u> with complete restaging 1 mo later, before being included in the waiting list (see recommendation 2.6b).	2B	29,30
2.6b	In patients beyond Milan but within “Up-to-7” without radiological response after <u>locoregional therapy</u> (partial or complete as defined by RECIST 1.1 criteria) and progressive increase of serum AFP despite locoregional therapy, LT should be contraindicated.	2C	31-33
2.7	The above-referred recommendations do not apply to downstaging strategies. Given the <u>heterogeneity and complexity</u> of the scientific evidence around this practice, a dedicated consensus document is warranted.	2C	N/A



... at similar (active) tumor burden

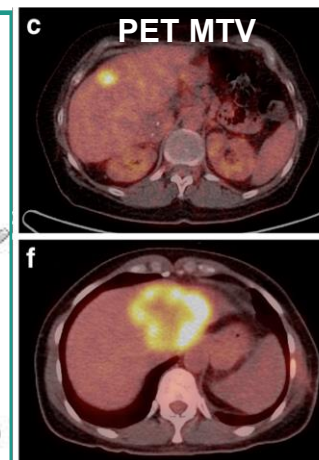
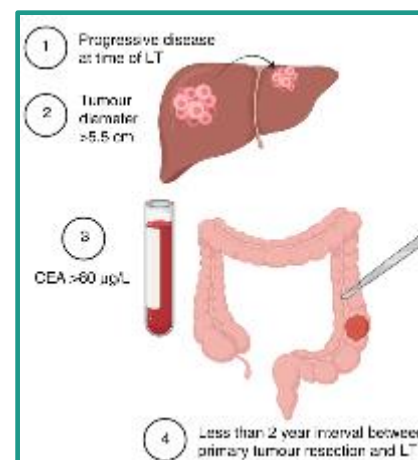
Mazzaferro V et al. Transplant Oncology (Ed M Abdelrahim) 2024; Adam R et al. Lancet 2024; Dueland S et al. JAMA Surg. 2023; Bonney GK et al. Lancet Gastro Hep 2021;

## Primary liver cancer (HCC)



## Liver mets (CRLM)

### Oslo Score



### TransMet criteria

Supplementary Table S2 (online only): Eligibility criteria

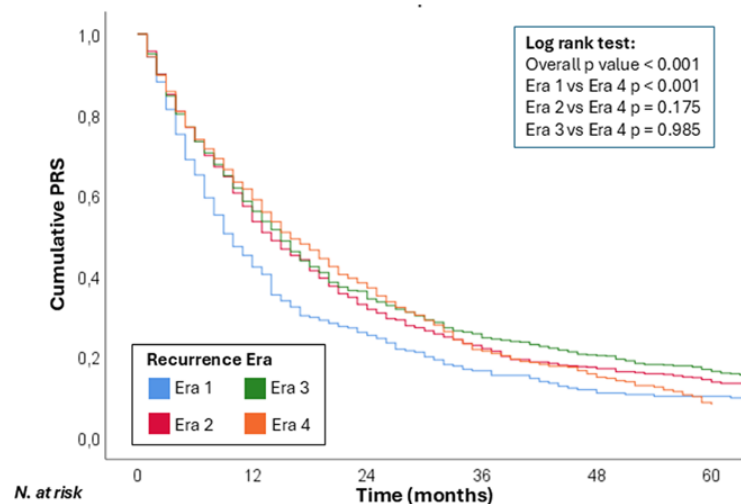
Eligibility	Details
Inclusion criteria	<ul style="list-style-type: none"> <li>- ≥ 18 and ≤ 65 years</li> <li>- Good performance status, ECOG 0 or 1 (39)</li> <li>- Histologically proved adenocarcinoma in colon or rectum</li> <li>- BRAF wild-type CRC on primary tumor or hepatic metastases</li> <li>- High standard oncological surgical resection of the primary defined by: <ul style="list-style-type: none"> <li>o Safe margin of resection</li> <li>o Curative resection of primary tumor according to oncological principles</li> <li>o TNM adequate staging</li> </ul> </li> <li>- Absence of local recurrence on colonoscopy performed in the 12 months prior to inclusion (except in case of primary resection &lt; 12 months)</li> <li>- Confirmed non resectable liver metastases of colorectal cancer by the validation committee</li> <li>- ≥ 3 months of tumor control during the last chemotherapy line: Stable or Partial Response on RECIST criteria (40)</li> <li>- ≤ 3 lines of chemotherapy for metastatic disease</li> <li>- CEA &lt; 80 ng/mL or a decrease ≥ 50% of the highest serum CEA levels observed during the disease</li> <li>- Absence of extrahepatic tumor localisation according to CT scan and PET-CT</li> <li>- Renal function should be within the normal limits</li> <li>- No need for extra-renal purification procedure, hemodialysis or kidney transplantation associated (nephrological evaluation)</li> <li>- A platelet count &gt; 80,000/mm<sup>3</sup></li> <li>- White blood cell count &gt; 2500/mm<sup>3</sup></li> <li>- Eligible for both treatment groups</li> <li>- Signed informed consent and expected cooperation of the patient for the treatment and follow up</li> </ul>
Non-inclusion criteria	<ul style="list-style-type: none"> <li>- Participation refusal</li> <li>- No health insurance facilities</li> <li>- General contraindication to LT (Severe cardiopulmonary disease or other life-limiting coexisting medical conditions, extrahepatic malignancy, active alcohol or substance abuse, active infection or uncontrolled sepsis, lack of psychosocial support or inability to comply with medical treatment)</li> <li>- Other malignancies either concomitant or within 5 years before liver transplantation</li> <li>- Patients not having received high standard oncological surgery of the primary CRC according to recommended guidelines*</li> <li>- Prior extra hepatic metastatic disease or local relapse</li> <li>- Pregnancy at the time of inclusion</li> </ul>

# Post-recurrence Survival after Liver Transplantation for Hepatocellular Carcinoma

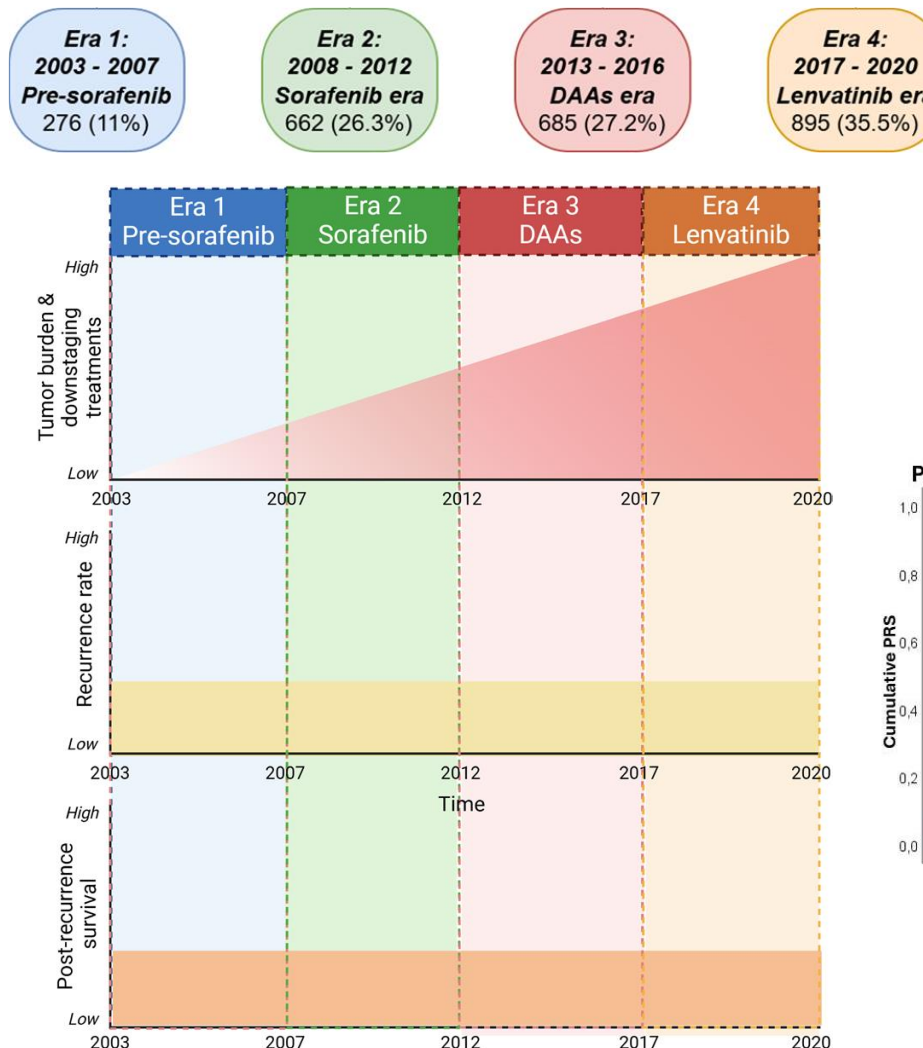
Scientific Registry of Transplant Recipients (SRTTs)  
2003 - 2020 : **2518 patients with LT for HCC**

At multivariable analysis, only time to recurrence <24 months and G3 HCC were associated with PRS, while recurrence era was not.

Post-recurrence survival after LT for HCC

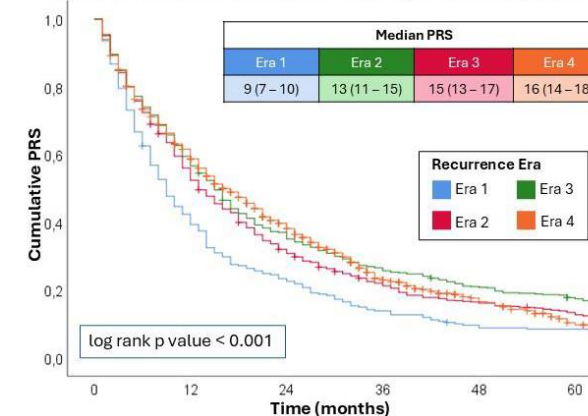


While **PRS** after LT for HCC has improved with respect to the early days of inception of transplant oncology, it has **not improved during the last 2 decades**



There has been an **increase of tumor burden and neoadjuvant treatments in later eras**, without a **significant change in post-transplant recurrence survival**

Post-recurrence survival in Milan-IN at transplant



PRS has significantly improved in patients with Milan-IN tumors at LT



## LDLT as a model for non-restrictive criteria for LT in HCC

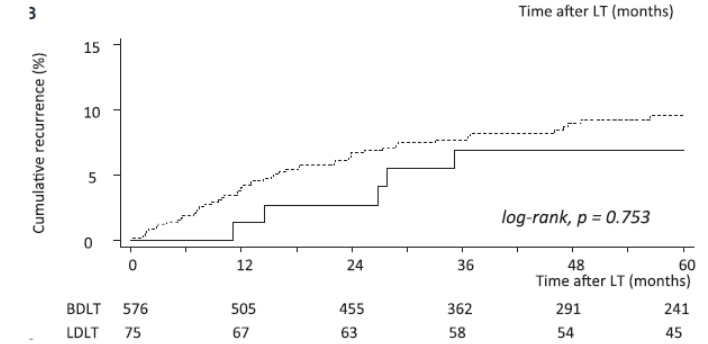
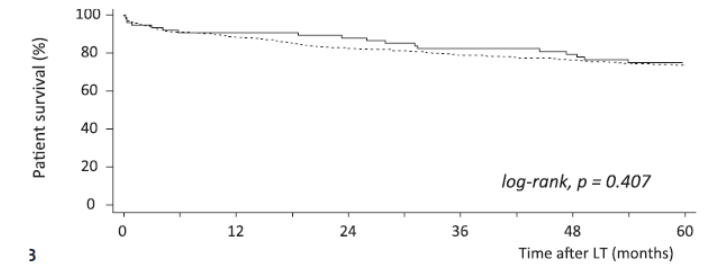
TABLE 5. Risk of HCC Recurrence After Liver Transplantation, Fine and Gray Competing Risks Regression Model (n = 651)

		Univariate Analysis		Multivariate Analysis			
		SHR (95% CI)	P	Model A*		Model B*	
				SHR (95% CI)	P	SHR (95% CI)	P
Age, years	Per 1 year increase	0.98 (0.94;1.01)	0.152	0.97 (0.94;1.01)	0.108	0.98 (0.94;1.01)	0.224
Sex	Male	1.44 (0.62;3.34)	0.395	1.32 (0.52;3.38)	0.559	1.35 (0.54;3.33)	0.521
Underlying liver disease	Viral	1 (reference)		1 (reference)		1 (reference)	
	Alcohol	0.85 (0.48;1.52)	0.590	0.97 (0.51;1.82)	0.917	1.00 (0.52;1.93)	0.992
	Viral + alcohol	1.12 (0.43;2.92)	0.816	0.85 (0.30;2.43)	0.766	1.05 (0.37;3.00)	0.926
	Others	1.47 (0.61;3.51)	0.392	1.41 (0.52;3.82)	0.495	1.67 (0.60;4.61)	0.323
Pre-transplant treatment	Radiofrequency/TACE	1 (reference)		1 (reference)		1 (reference)	
	Surgery/combined	1.24 (0.31;5.01)	0.762	1.02 (0.34;3.03)	0.972	1.22 (0.40;3.71)	0.727
	None	0.97 (0.57;1.66)	0.909	0.88 (0.45;1.70)	0.699	0.90 (0.47;1.73)	0.760
ABO blood group	A	1 (reference)		1 (reference)		1 (reference)	
	AB	1.17 (0.41;3.35)	0.775	0.86 (0.25;2.94)	0.811	0.92 (0.29;2.93)	0.888
	B	0.50 (0.17;1.43)	0.194	0.41 (0.13;1.30)	0.131	0.46 (0.15;1.36)	0.159
	O	0.77 (0.41;1.45)	0.421	0.74 (0.36;1.53)	0.414	0.72 (0.34;1.53)	0.396
Child-Pugh class	AB	1 (reference)		1 (reference)		1 (reference)	
	C	1.19 (0.61;2.32)	0.613	1.07 (0.43;2.66)	0.888	1.14 (0.48;2.74)	0.764
MELD score at listing	Per 1 point increase	1.00 (0.96;1.05)	0.911	—		—	
	<15	1 (reference)		1 (reference)			
	15-25	1.25 (0.65;2.41)	0.508	1.11 (0.47;2.59)	0.817	1.09 (0.47;2.52)	0.837
	≥25	1.68 (0.64;4.40)	0.294	1.45 (0.46;4.59)	0.527	1.57 (0.53;4.64)	0.413
Waiting time on list, months	Per 1 month increase	0.99 (0.94;1.04)	0.780	1.00 (0.96;1.04)	0.972	1.00 (0.95;1.05)	0.969
Graft type (BDLT /LDLT)	BDLT group	1 (reference)		1 (reference)		1 (reference)	
	LDLT group	0.91 (0.42;1.96)	0.806	1.64 (0.50;5.34)	0.415	1.50 (0.45;4.92)	0.507
Donor age	≥60 y	1.31 (0.74;2.34)	0.356	1.15 (0.61;2.16)	0.661	1.33 (0.70;2.50)	0.379
Cold ischemia time, hours	Per 1 hour increase	0.99 (0.92;1.06)	0.768	0.97 (0.86;1.08)	0.560	0.96 (0.86;1.07)	0.492
Transfusion	Per 1 unit increase	1.01 (0.98;1.04)	0.501	1.01 (0.97;1.05)	0.589	1.01 (0.97;1.05)	0.594
Microscopic vascular invasion		2.61 (1.57;4.33)	<0.001	—		—	
Macroscopic vascular invasion		3.45 (1.94;6.13)	<0.001	2.21 (1.21;4.06)	0.010	2.26 (1.26;4.08)	0.007
Satellite nodules		2.29 (1.38;3.82)	0.001	1.36 (0.77;2.40)	0.292	1.31 (0.72;2.38)	0.384
Milan criteria (explanted liver)	Out	3.52 (2.03;6.10)	<0.001	2.81 (1.54;5.12)	0.001	—	
AFP model score (explanted liver)	>2	3.54 (2.10;5.97)	<0.001	—		2.71 (1.48;4.95)	0.001
Edmondson grade I-II vs. III-IV	III-IV	2.21 (1.26;3.86)	0.006	1.70 (0.93;3.10)	0.086	1.69 (0.93;3.10)	0.087

AFP indicates alpha-fetoprotein; BDLT, brain-dead donor liver transplantation; CI, confidence interval; HR, hazard ratio; LDLT, living donor liver transplantation; MELD, Model for end stage liver disease; SHR, sub-hazard ratio; TACE, transarterial chemoembolization.

Bolded results are significant at the  $P < 0.05$  level.

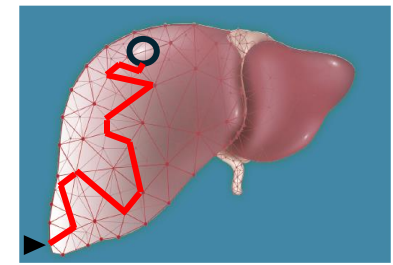
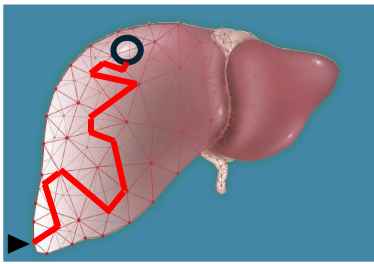
\*Two alternative multivariate models were built to prevent colinearity between Milan and AFP model score, entering (A) Milan criteria or (B) AFP model score.



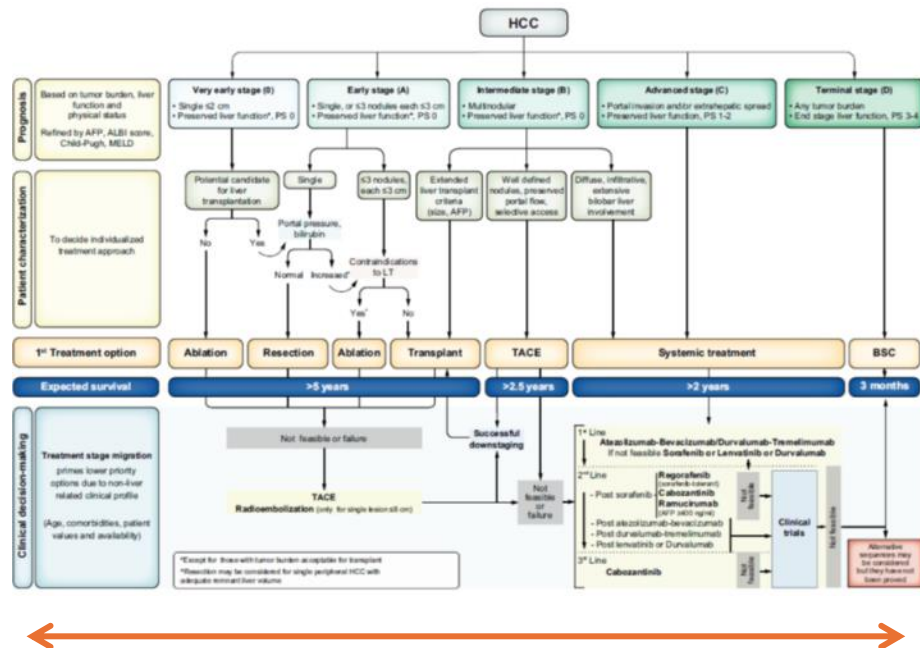
BDLT drop-out rate: 20.7%  
LDLT drop-out: none (0%)

Graft type was not associated with risk of recurrence

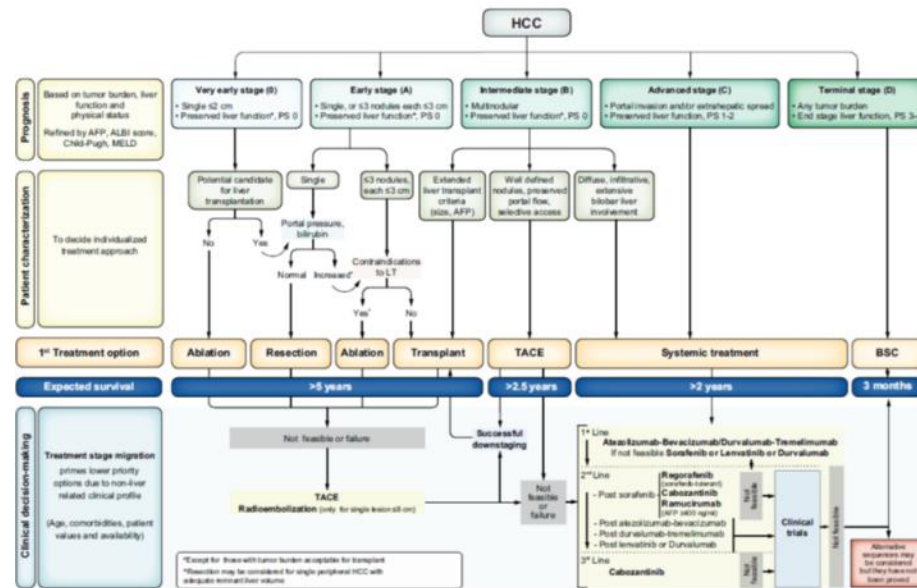
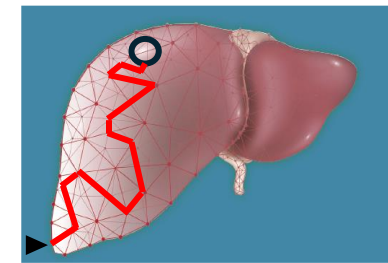
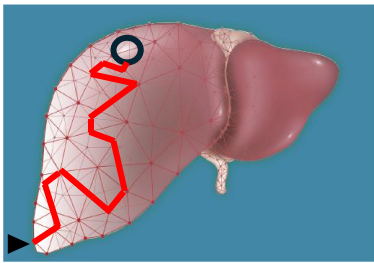
Independent predictors of recurrence were:  
in Model A: macroscopic vascular invasion [HR 2.21],  
and **tumor exceeding the Milan criteria [HR 2.81]**; (ii)  
in Model B: macroscopic vascular invasion [HR 2.26]  
and **AFP model score >2 [HR 2.71]**



Thanks to technologic advancements, big data analysis,  
and powerful networks we are entering an  
**Era of Translation**  
in modelling outcome predictions and decision-making



Exclude liver transplant if	Comorbidities, severe frailty, 1 biological age	STOP	STOP	Extended criteria, TAFP or PVKA-II, stable disease or progressive disease	—	LDLT or DCD unavailable, 1 expected waiting time, technical constraints
Exclude liver resection if:	Comorbidities, severe frailty	STOP	STOP	>Three nodules, critical location	MELD >10, 1 CRPH, Child-Pugh class >A6, & liver remnant	Technical constraints
Exclude percutaneous ablation if	Severe comorbidities	STOP	STOP	Size >3 cm, >five nodules, critical location	Child-Pugh class >B7, high-risk of bleeding	Technical constraints
Exclude videolaparoscopic ablation if	Severe comorbidities	STOP	STOP	Size >4 cm, >five nodules, critical location	Child-Pugh class >B9	Technical constraints
Exclude intra-arterial therapies if	Severe comorbidities	STOP	STOP	Size >5 cm (TACE), diffuse infiltrative, intrahepatic PVT (TACE)	Child-Pugh class >B7	Technical constraints, unavailability (high costs)
Exclude systemic therapy if	Severe comorbidities	STOP	—	—	Child-Pugh class >B7	Cost ineffective
Best supportive care	—	—	—	—	—	—



Exclude liver transplant if	Comorbidities, severe frailty, 1 biological age	STOP	STOP	Extended criteria, TAFP or PVKA-II, stable disease or progressive disease	—	LDLT or DCD unavailable, 1 expected waiting time, technical constraints
Exclude liver resection if:	Comorbidities, severe frailty	STOP	STOP	>Three nodules, critical location	MELD >10, 1 CRPH, Child-Pugh class >A6, & liver remnant	Technical constraints
Exclude percutaneous ablation if	Severe comorbidities	STOP	STOP	Size >3 cm, >five nodules, critical location	Child-Pugh class >B7, high-risk of bleeding	Technical constraints
Exclude videolaparoscopic ablation if	Severe comorbidities	STOP	STOP	Size >4 cm, >five nodules, critical location	Child-Pugh class >B9	Technical constraints
Exclude intra-arterial therapies if	Severe comorbidities	STOP	STOP	Size >5 cm (TACE), diffuse-infiltrative, intrahepatic PVT (TACE)	Child-Pugh class >B7	Technical constraints, unavailability (high costs)
Exclude systemic therapy if	Severe comorbidities	STOP	—	—	Child-Pugh class >B7	Cost-ineffective
Best supportive care	—	—	—	—	—	—

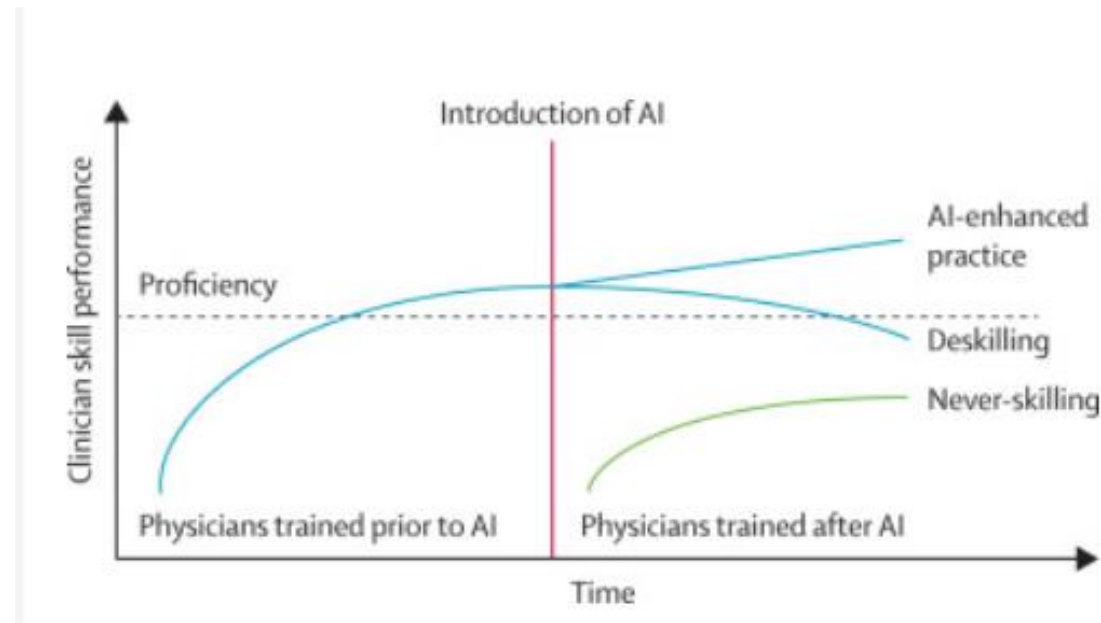
Domain-specific excellence is emerging, with vast potential for translational progress. In an era in which big, deep, and longitudinal data are available, **relying on a simple, singular or binary measure to define risk is simplistic**. If all dimensions of data were integrated, just think how much better we could identify risk group in an era in which treatments are develop and people are aware.



# THE LANCET

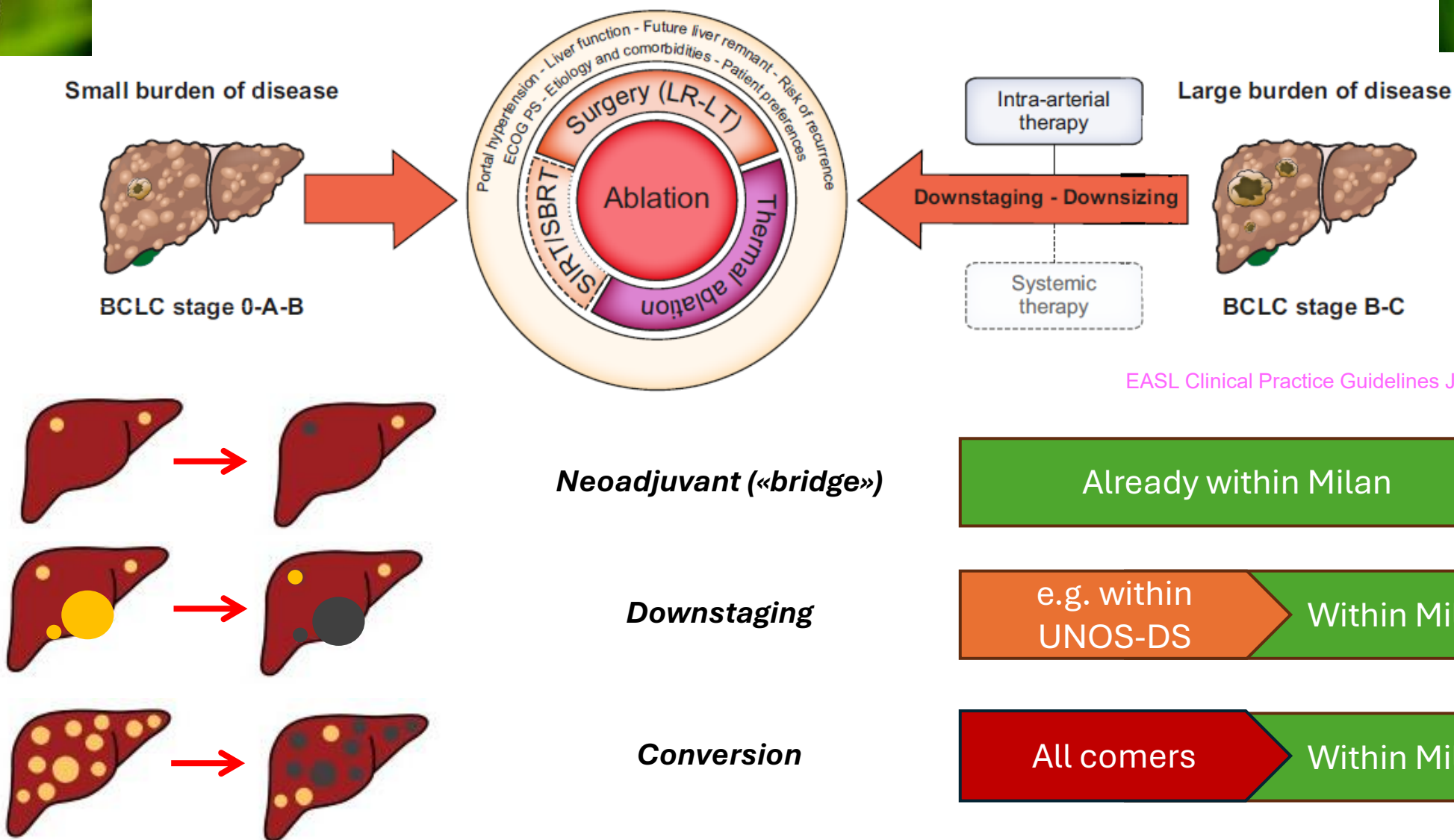
## Preserving clinical skills in the age of AI assistance

[Tyler M Berzin](#)<sup>a</sup> · [Eric J Topol](#)<sup>b</sup>



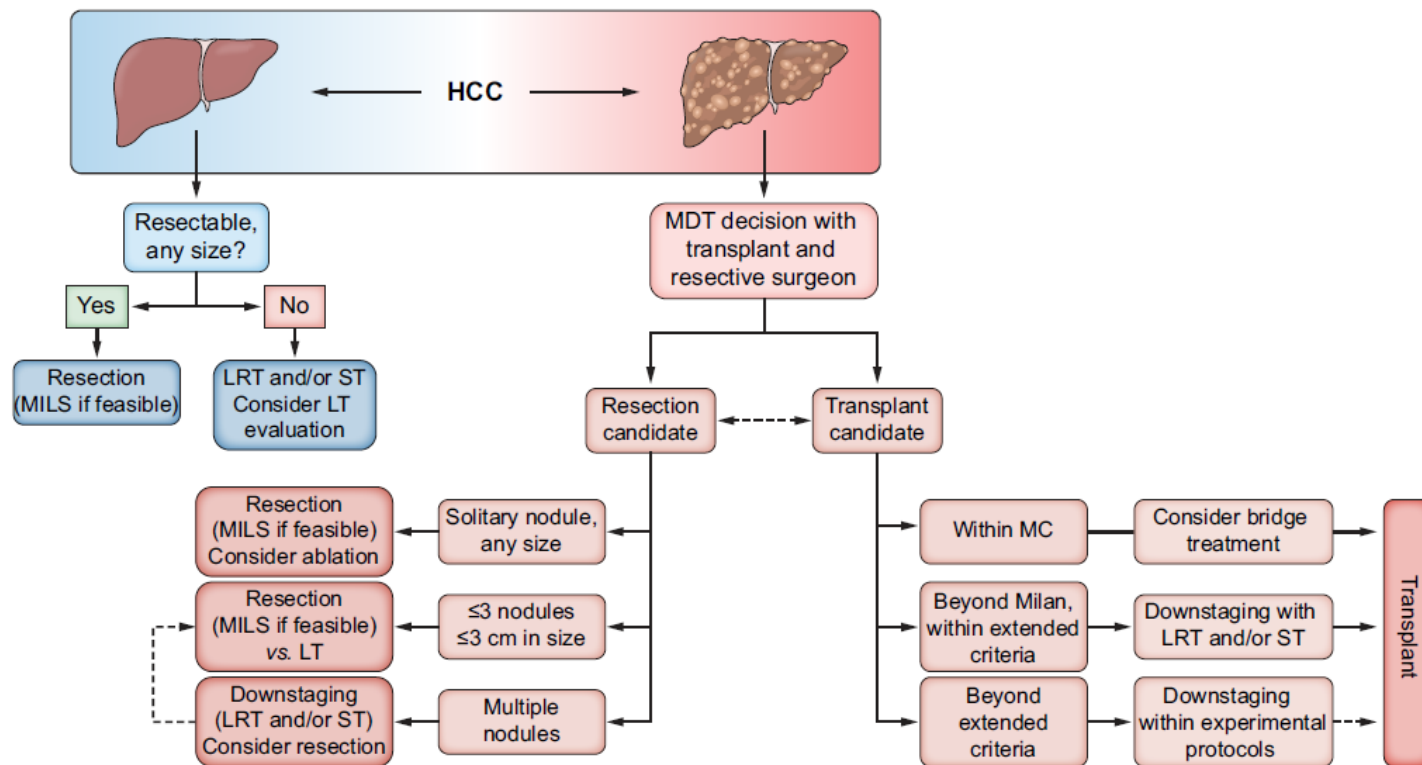
As A.I. assumes a growing role in clinical practice, concerns is mounting that off-load clinical tasks and reasoning will lead to **loss of skills (deskilling)** adopting errors or bias from A.I. (mis-skilling), or failure to achieve competence (never skilling)

The Translation of Transplant indication in HCC



## Translation of borderline resectable, ALPPS, staged hepatectomies for HCC?

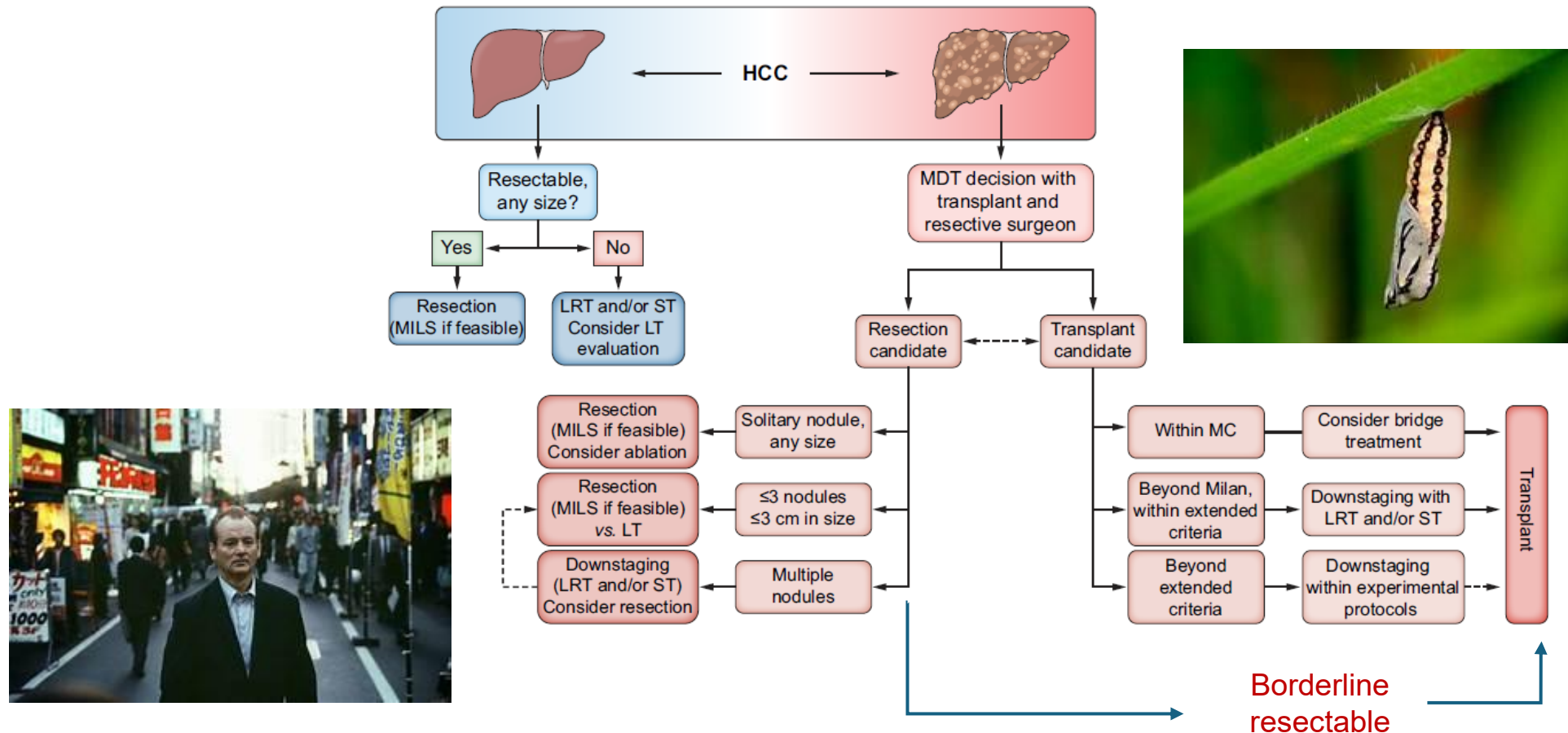
- Heterogeneities in defining surgical feasibility and surgical futility influence indication, patient selection and outcome





# Translation of borderline resectable, ALPPS, staged hepatectomies for HCC?

- Heterogeneities in defining surgical feasibility and surgical futility influence indication, patient selection and outcome



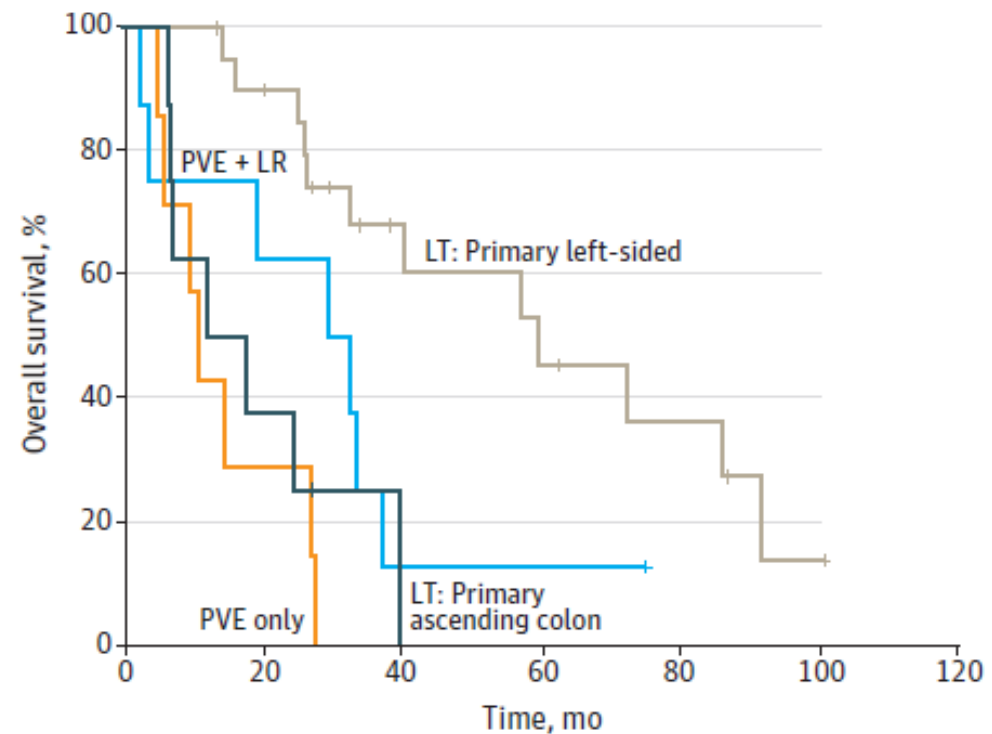
## LT vs. PVE followed by liver resection (PVE+LR)

50 LT (2006-2019) at Oslo University compared with a retrospective cohort of 53 PVE+LR (2006-2015)

- Similar selection criteria
- **Different tumor load at inception**

High tumor load:

25.8% in the PVE+LR group: 58.0% in the LT group



No. at risk	0	20	40	60	80	100
LT: ascending	8	3	0	0	0	0
LT: left	21	18	9	6	4	1
PVE + LR	8	5	1	1	0	0
PVE only	7	2	0	0	0	0

✓ **LT yields a longer overall survival among selected patients with advanced CRLM with high tumor burden with respect to PVE followed by liver resection**

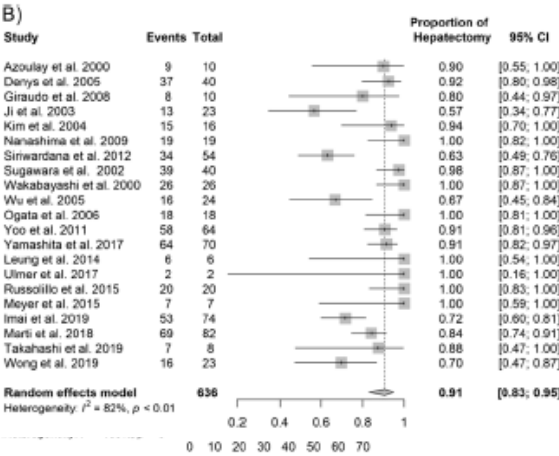
- Right-sided primary tumor is a distinct negative prognostic factor (among other factors are more pN+)
- Patients with <9 liver metastases <5.5 cm in diameter, may obtain long OS also with LR following the PVE
- Patients with high liver tumor load benefit from LT even if they are resectable
- Patients who do not respond to PVE may be evaluated for LT.

# The Transition of complex liver resection to transplantation

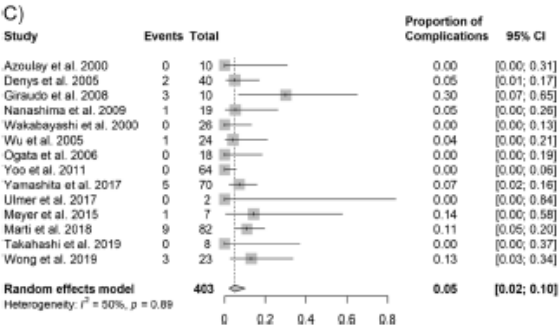
Systematic reviews of future liver remnant percent hypertrophy, proportion undergoing hepatectomy and proportion with major complications following PVE, ALPPS, and RL

ALPPS Versus Portal Vein Embolization for Hepatitis-related Hepatocellular Carcinoma  
*A Changing Paradigm in Modulation of Future Liver Remnant Before Major Hepatectomy*

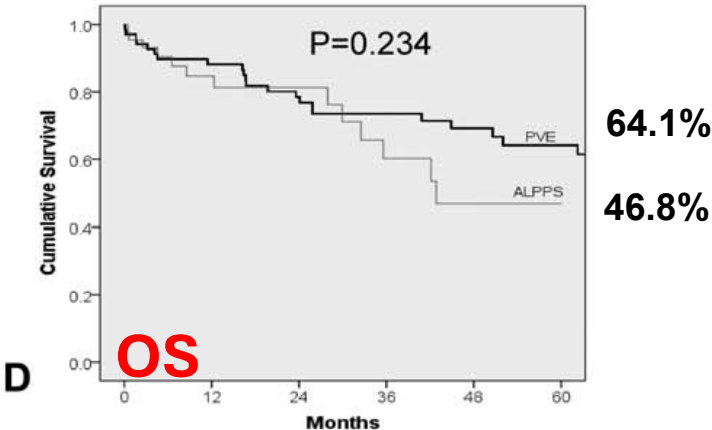
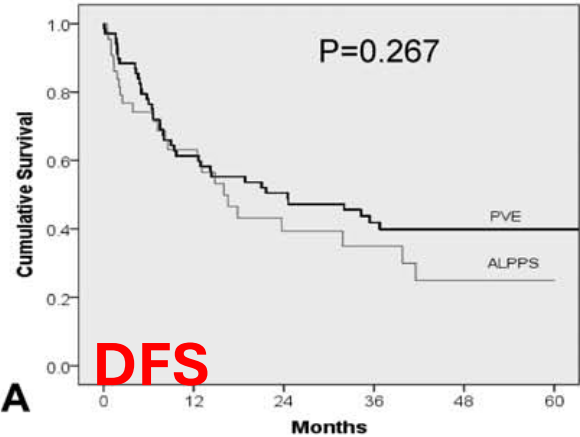
Proportion undergoing hepatectomy



Proportion with major complications



46 ALPPS vs 102 PVE  
Cirrhosis 50%  
Median size: 8.5 cm  
Median n: 1 (1-3)



Failure rate:

- ALPPS: 2.2%
- PVE: 32.3%

Morbidity:

- ALPPS: 30.4%
- PVE: 20.7%

Mortality:

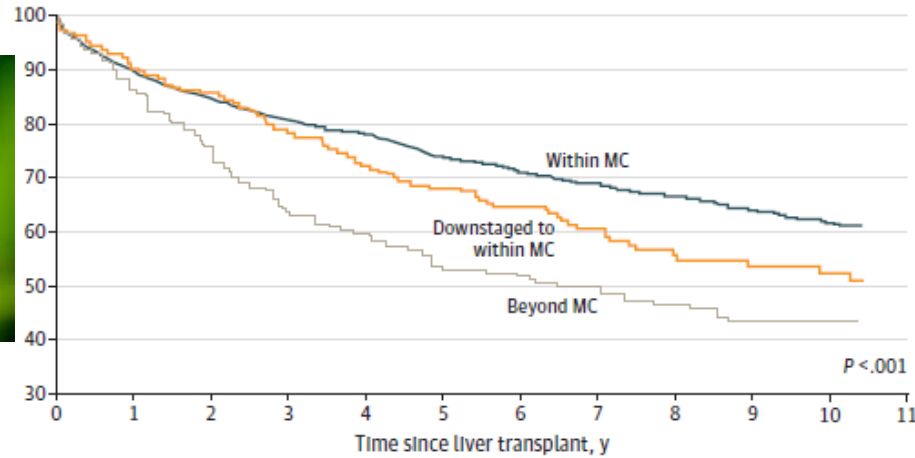
- ALPPS: 6.5%
- PVE: 5.8%

PVE: 91% completed with 5% DCC > 3



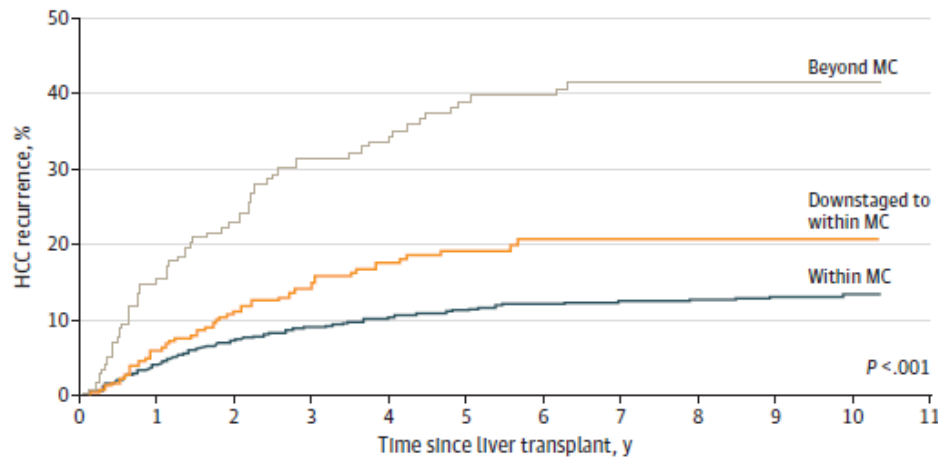
# The Translation of complex resective liver surgery to the Transplant perspective

**A** Overall survival among patients with HCC after liver transplant by subgroup

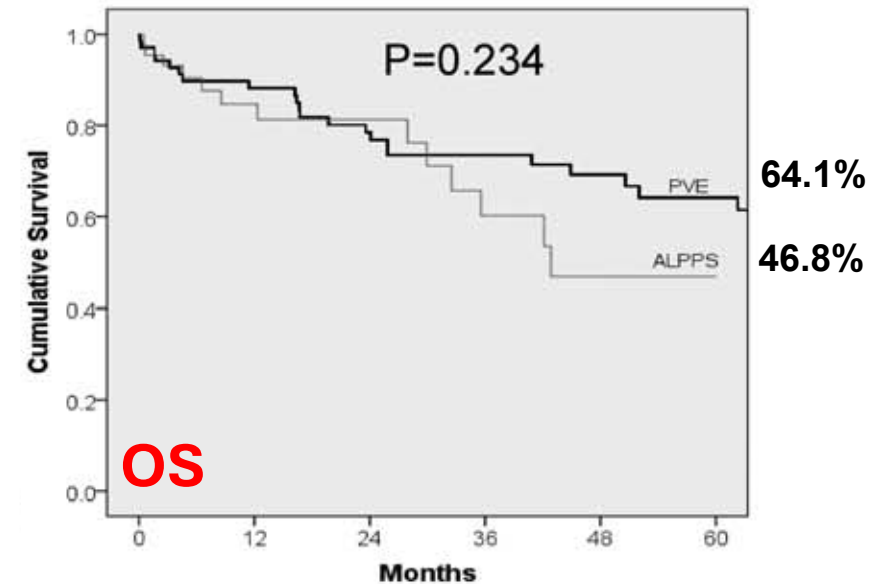


No. at risk	2122	1808	1638	1453	1224	985	784	634	507	384	272
Within MC	2122	1808	1638	1453	1224	985	784	634	507	384	272
Downstaged to within MC	341	293	267	225	185	136	104	80	58	46	40
Beyond MC	182	155	131	111	103	85	82	73	65	50	41

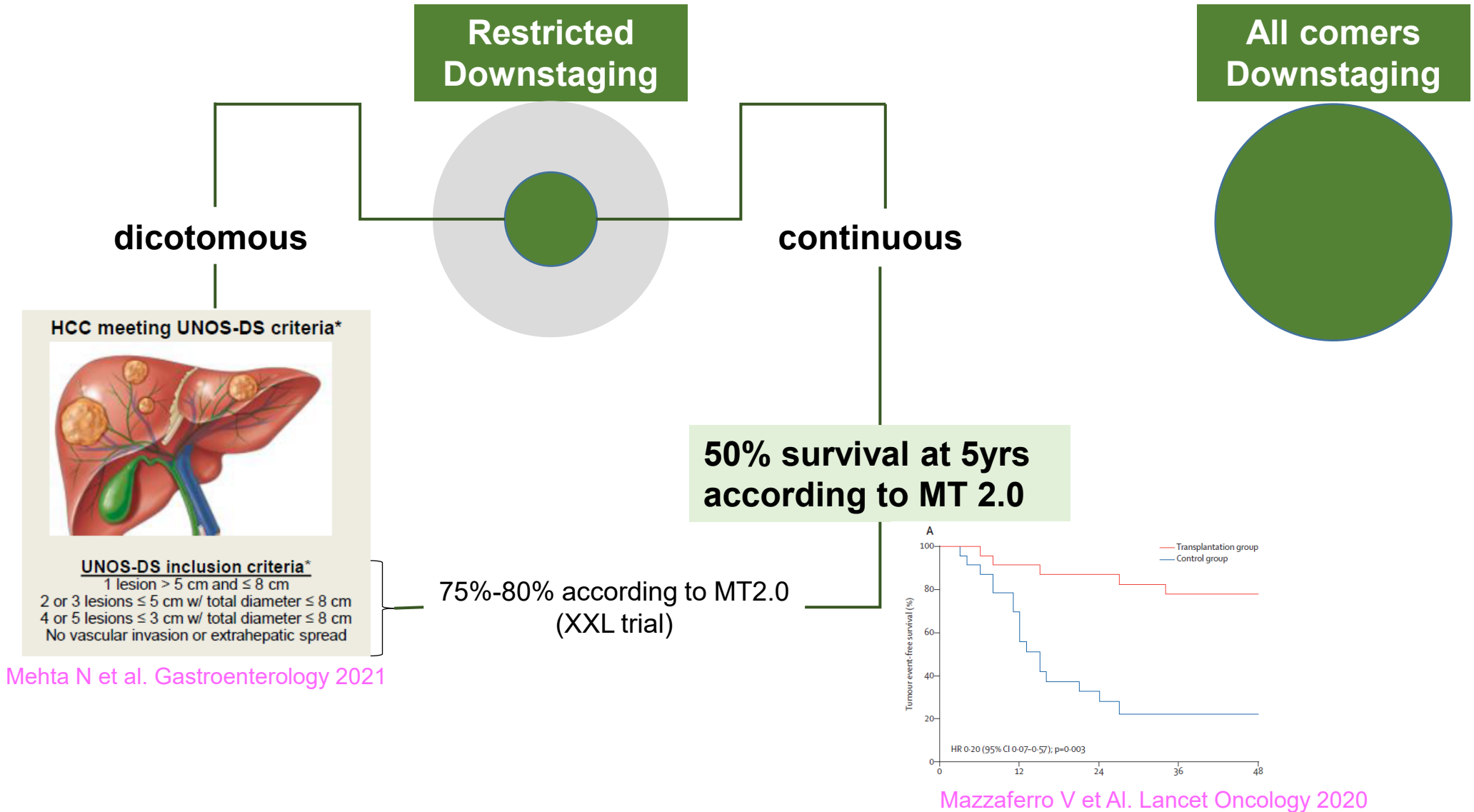
**B** Overall recurrence of HCC after liver transplant by subgroup



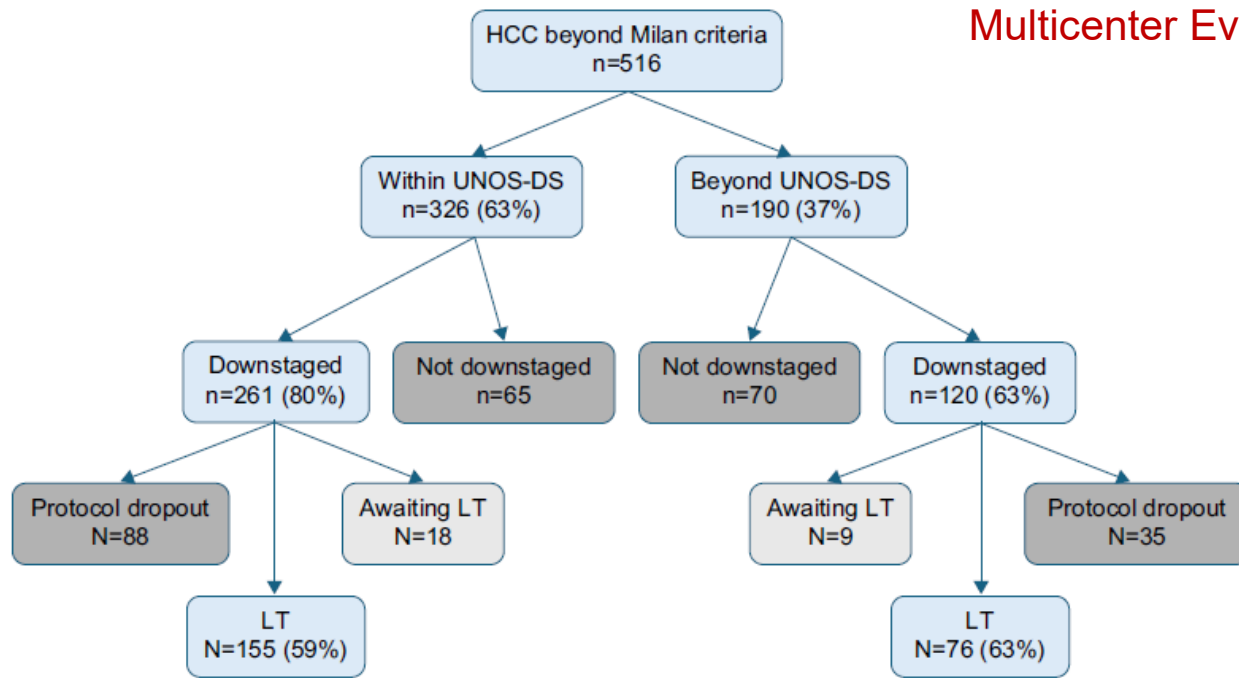
No. at risk	2122	1761	1575	1396	1172	942	747	603	408	368	262
Within MC	2122	1761	1575	1396	1172	942	747	603	408	368	262
Downstaged to within MC	341	280	245	209	173	127	96	73	55	43	37
Beyond MC	182	141	119	97	90	76	74	66	61	48	40



# The Translation of Downstaging boundaries for LT candidates with HCC



# Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT) consortium



## Predictors of successful downstaging

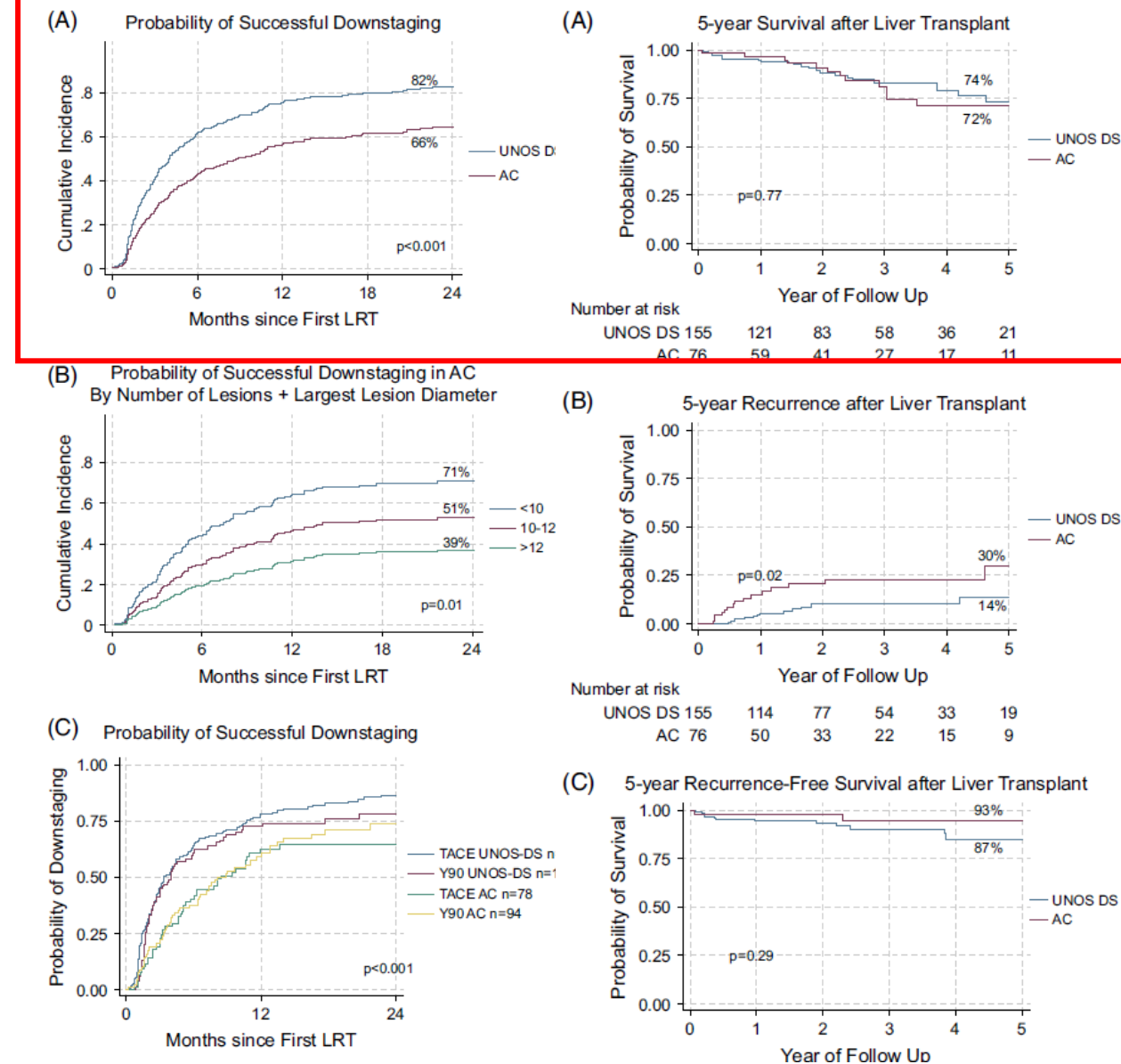
### Multivariable analysis

No. of lesions + largest lesion diameter (per unit)	0.84 (0.79–0.89)	<0.01
MASLD as Etiology (vs. hepatitis C)	0.72 (0.52–0.99)	0.048

## Predictors of inferior 5-year post-LT survival

### Multivariable analysis

Age (per y)	1.08 (1.02–1.14)	0.01
MASLD as etiology (vs. hepatitis C)	3.01 (1.08–8.39)	0.04
Explant microvascular invasion	3.77 (1.80–7.92)	<0.01



Despite higher HCC recurrence and lower ITT survival in AC, post-LT survival was comparable between UNOS-DS and all comers (AC), therefore LT after DS is feasible in AC. Defining an upper limit in tumor burden however is necessary



# Breakthrough innovation in HCC treatment

From Molecular based treatment



To Immunotherapy based treatment

Sharp trial: sorafenib vs. placebo

IMbrave150 trial: Atezo+Beva vs. sorafenib

Outcome	Sorafenib (N=299)	Placebo (N=303)	Hazard Ratio (95% CI)	P Value
Overall survival (mo)			0.69 (0.55–0.87)	<0.001
Median	10.7	7.9		
95% CI	9.4–13.3	6.8–9.1		
1-yr survival rate (%)	44	33		0.009
Time to symptomatic progression (mo)†			1.08 (0.88–1.31)	0.77
Median	4.1	4.9		
95% CI	3.5–4.8	4.2–6.3		
Time to radiologic progression (mo)			0.58 (0.45–0.74)	<0.001
Median	5.5	2.8		
95% CI	4.1–6.9	2.7–3.9		
Level of response (%)‡				
Complete	0	0		NA
Partial	2	1		0.05
Stable disease	71	67		0.17
Disease-control rate (%)§	43	32		0.002

	Atezolizumab plus bevacizumab (n = 326)	Sorafenib (n = 159)
Objective response, n (%) [95% CI]	97 (30) [25–35]	18 (11) [7–17]
Complete response, n (%)	25 (8)	1 (<1)
Partial response, n (%)	72 (22)	17 (11)
Stable disease, n (%)	144 (44)	69 (43)
Disease control rate, n (%)	241 (74)	87 (55)
Progressive disease, n (%)	63 (19)	40 (25)
Patients with ongoing response, n (%)	54 (56)	5 (28)
Duration of response, median (95% CI), months*	18.1 (14.6–NE)	14.9 (4.9–17.0)
Range, months	2.5–25.6†	2.5†–21.8

Cheng et al, J. Hepatol 2022

3-yr survival rates < 20%,  
DCR<50%, no CR

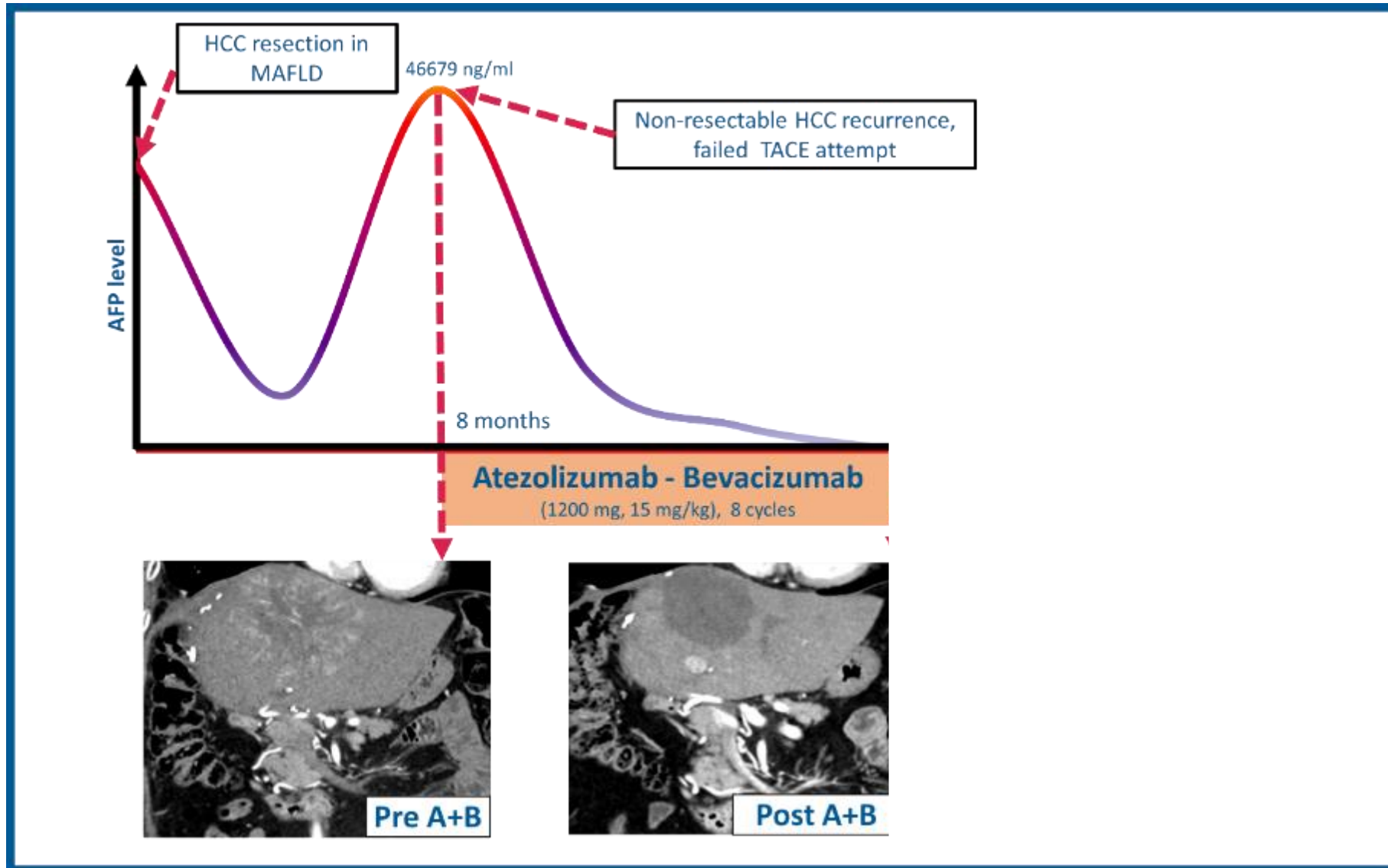


4-yr survival rates 30%,  
DCR 74%, CR 8%

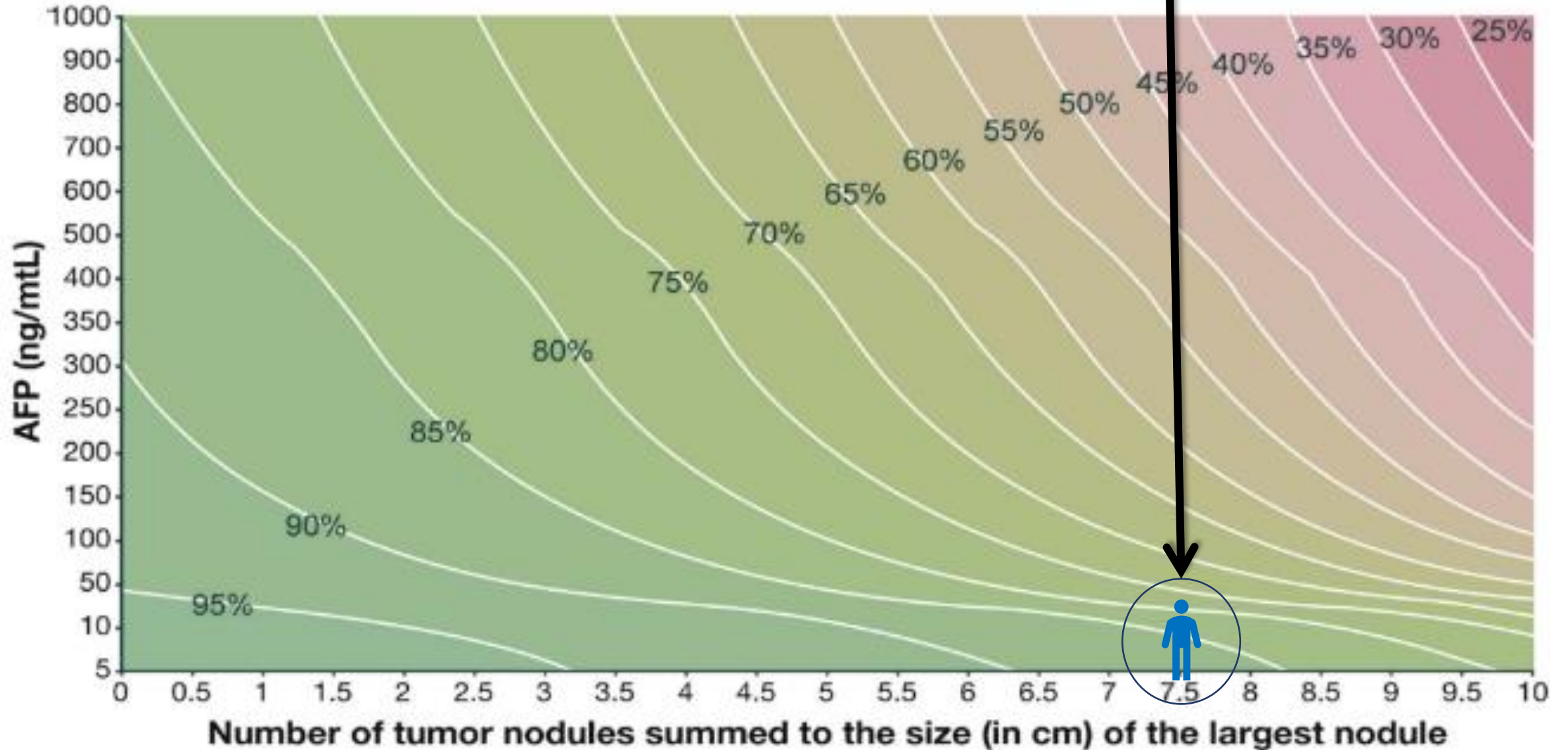
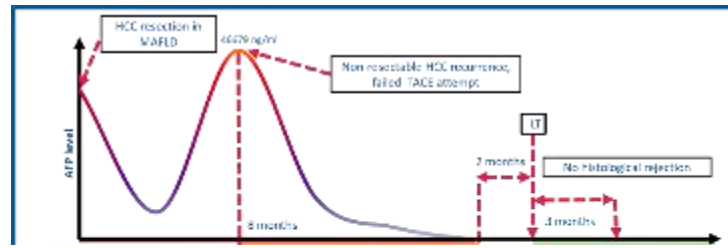
If immunotherapy produces deep and durable response



Why not offer liver transplantation and include immunotherapy in neoadjuvant protocols?



**[www.hcc-olt-metroticket.org](http://www.hcc-olt-metroticket.org)**





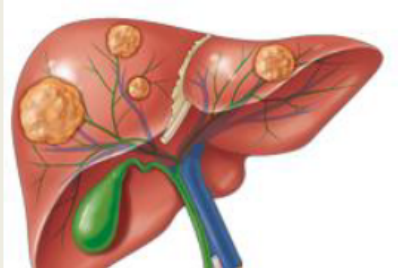
# The Translation of Downstaging boundaries for LT candidates with HCC

## Downstaging

**dicotomous**

**continuous**

HCC meeting UNOS-DS criteria\*



**UNOS-DS inclusion criteria\***

- 1 lesion > 5 cm and ≤ 8 cm
- 2 or 3 lesions ≤ 5 cm w/ total diameter ≤ 8 cm
- 4 or 5 lesions ≤ 3 cm w/ total diameter ≤ 8 cm
- No vascular invasion or extrahepatic spread

Mehta N et al. Gastroent- 2021  
Li M et al. JHepatol 2024

60% survival at 5yrs  
according to MT 2.0

## ImmunoXXL study

Intermediate-advanced  
HCC not-eligible to  
transplant after LRT

ICI

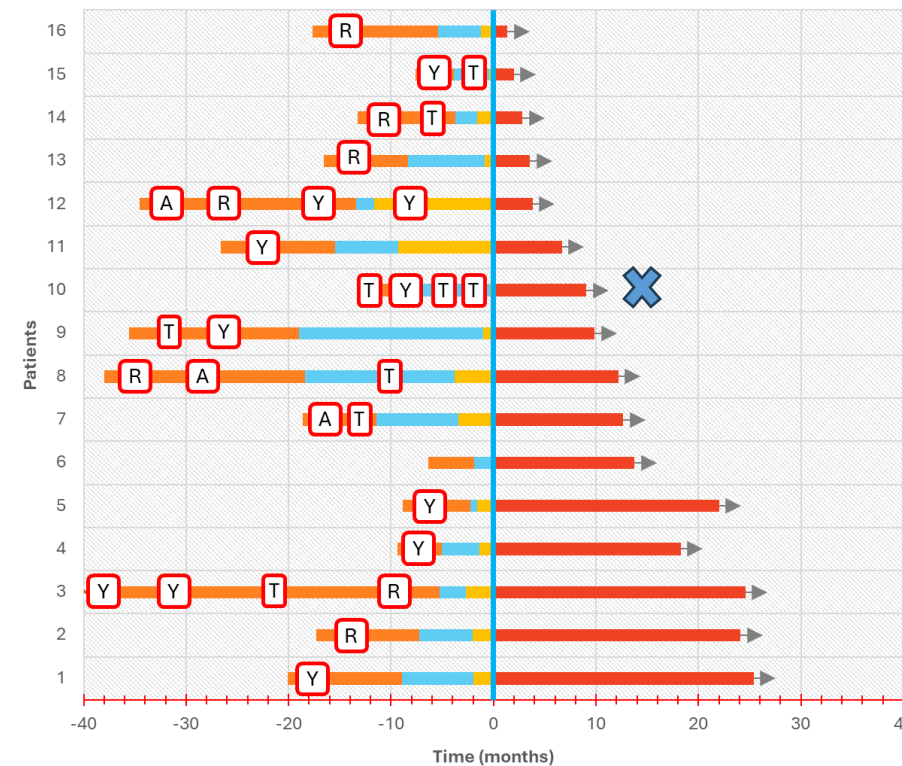
Downstaging to LT  
eligibility with ICI

LT

NCT05879328

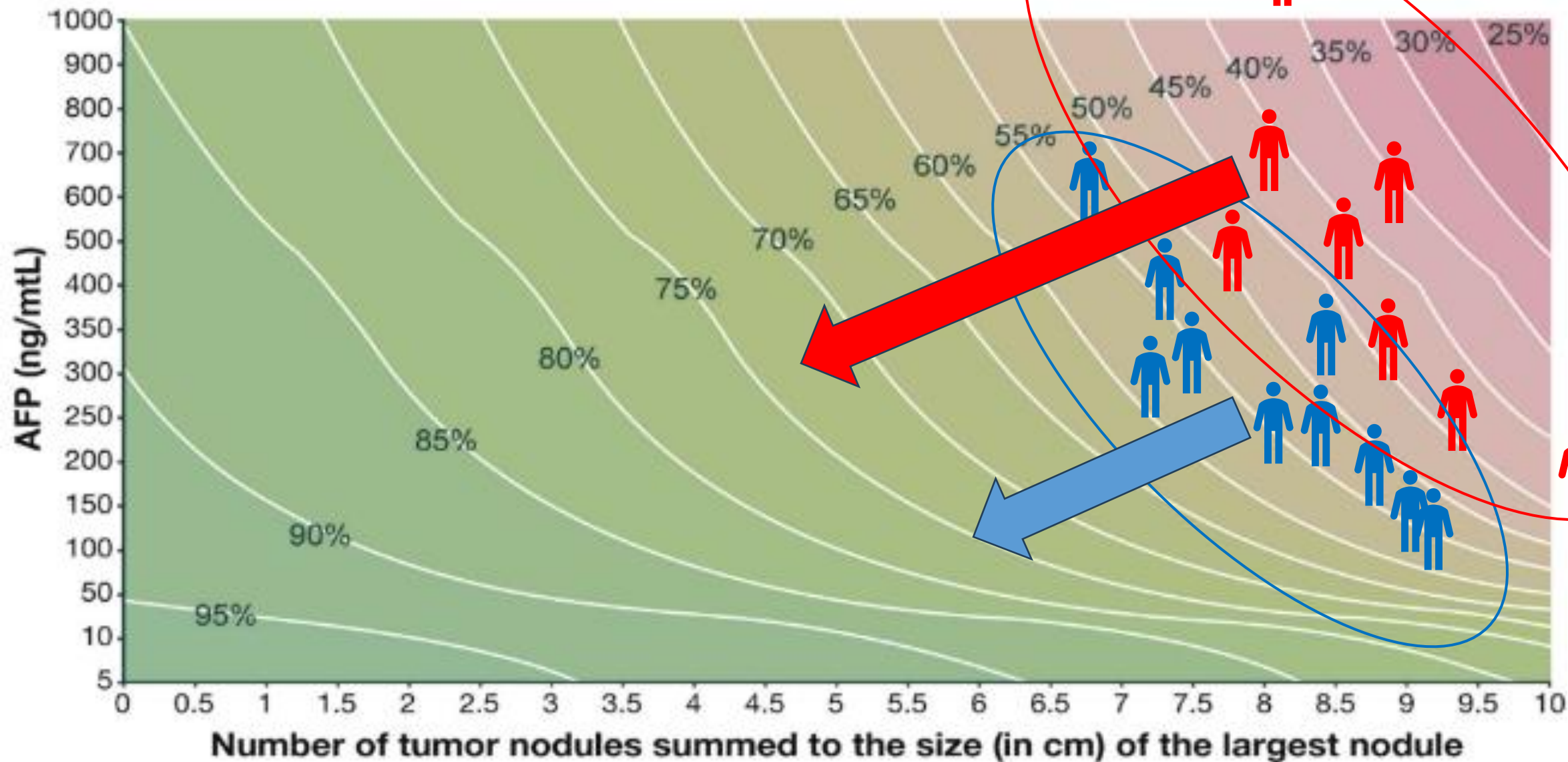
**all comers (?)**

ImmunoXXL Patient History Swimmer Plot



Tumor burden at inception  
in HCC patients downstaged to  
transplant eligibility

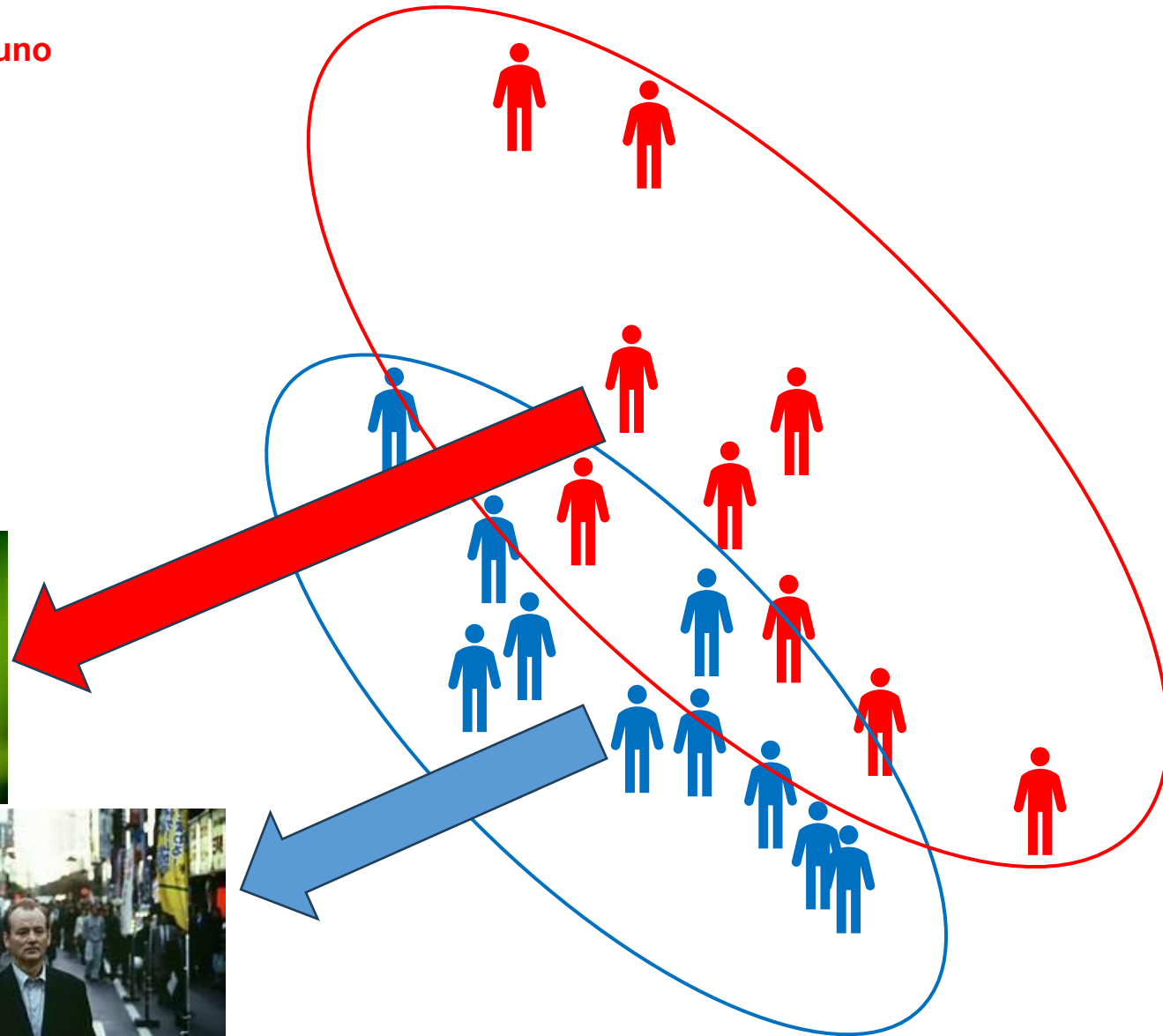
 **LRT+Immuno trial**  
 **LRT trial**



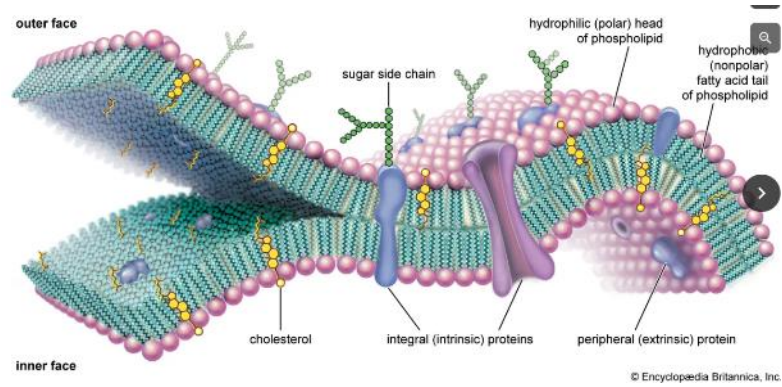
Tumor burden at inception  
in HCC patients downstaged to  
transplant eligibility



The concept of “**treatable tumor regression**” commonly referred to as therapeutic conversion - recognizes that profound tumor regression does not imply a return to an earlier baseline stage but creates a distinct clinical state requiring its own framework.



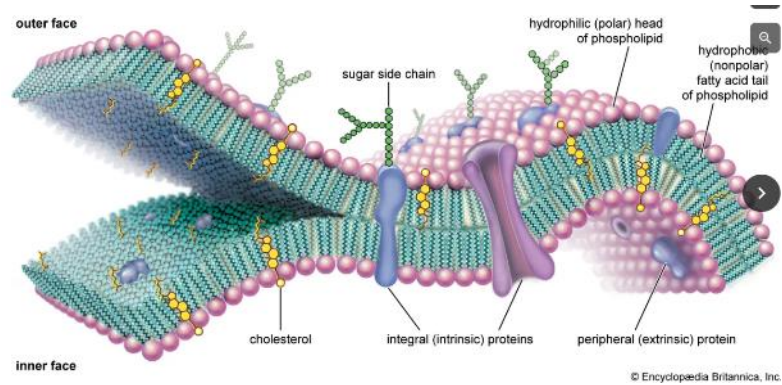
**In conclusion,**



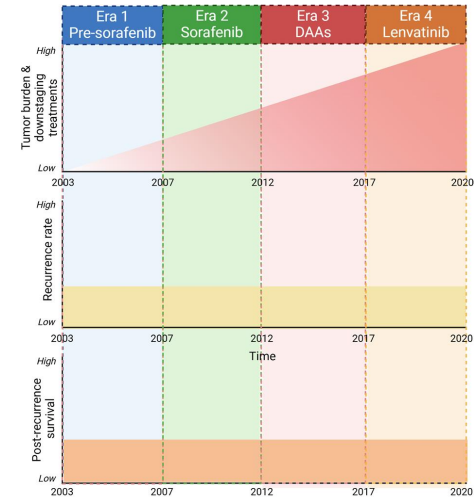
**Barriers** are essential to life



In conclusion,

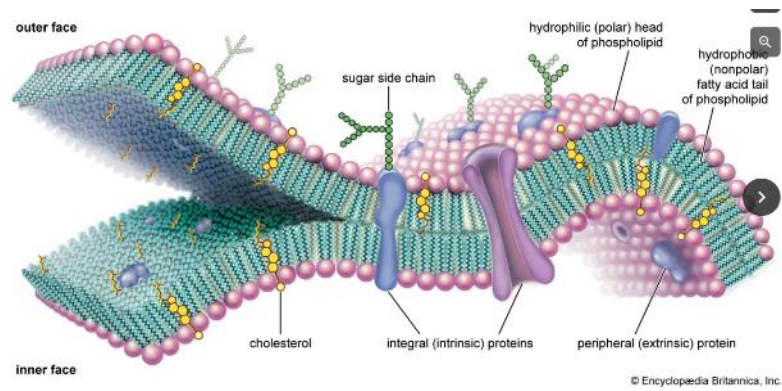


**Barriers** are essential to life

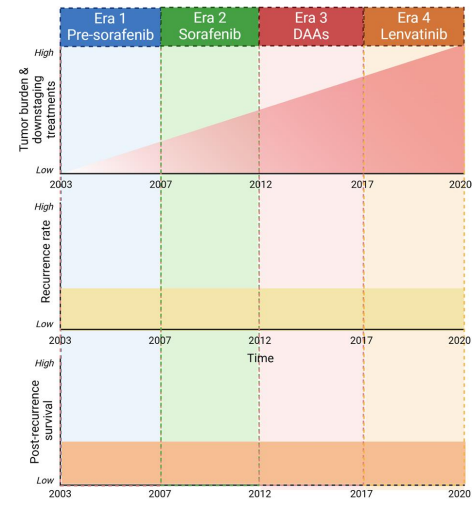


**Tumor burden** is a barrier that can be managed with non-transplant means

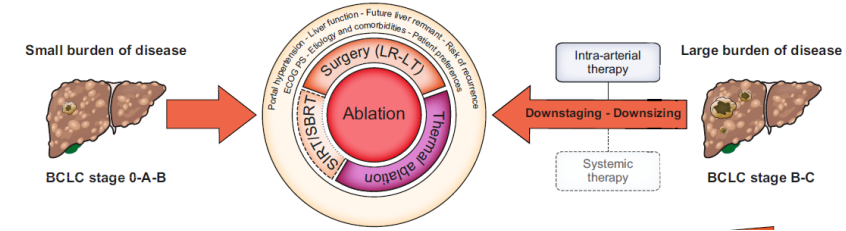
In conclusion,



Barriers are essential to life

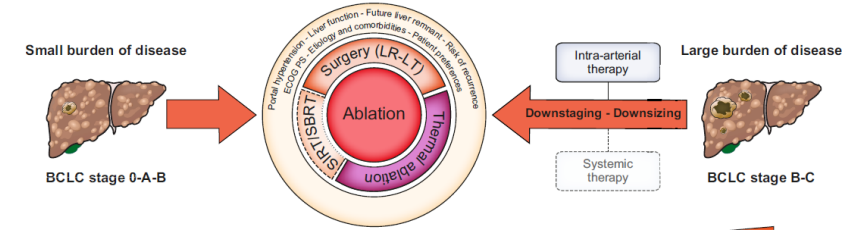
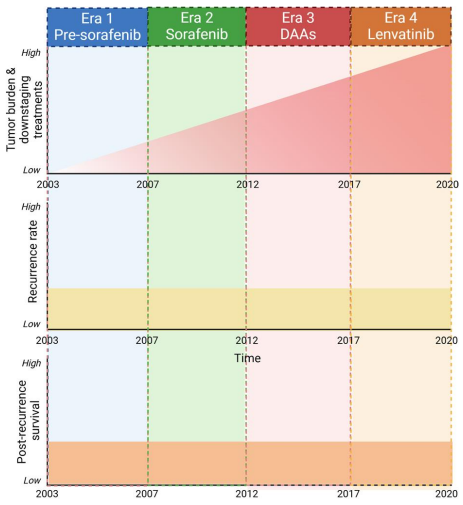
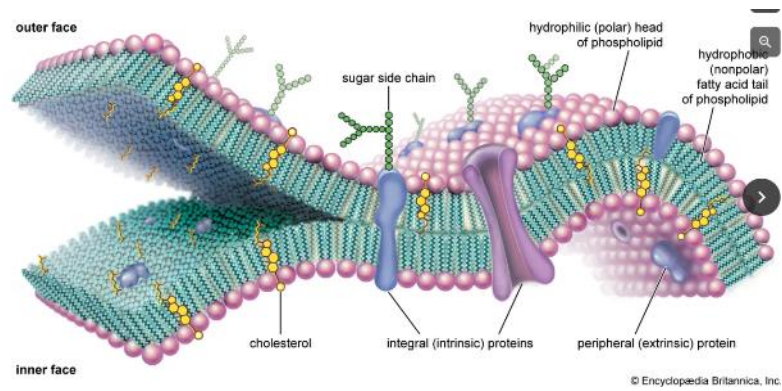


Tumor burden is a barrier that can be managed with non-transplant means



We are entering an era of Translation in outcome predictions and decision-making

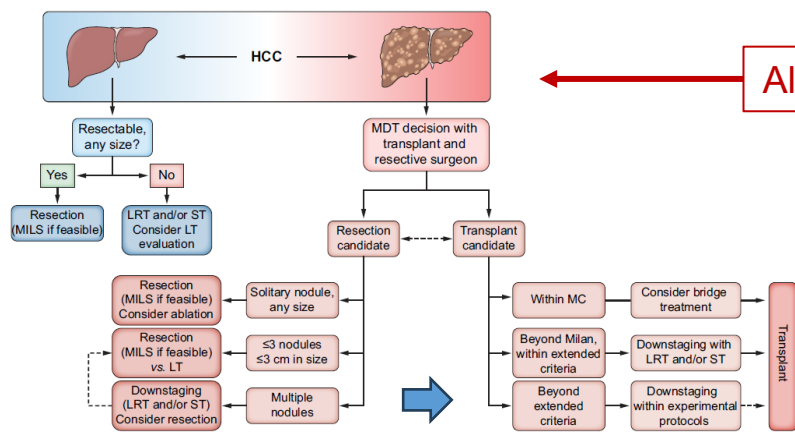
In conclusion,



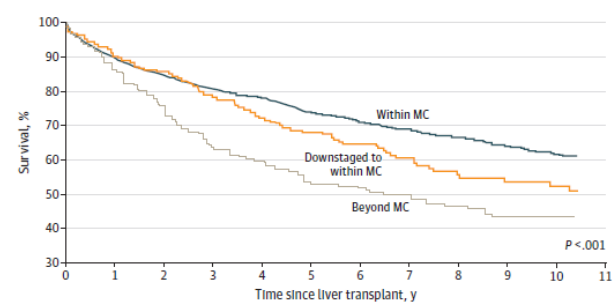
Barriers are essential to life

Tumor burden is a barrier that can be managed with non-transplant means

We are entering an era of Translation in outcome predictions and decision-making



All under restrictive criteria

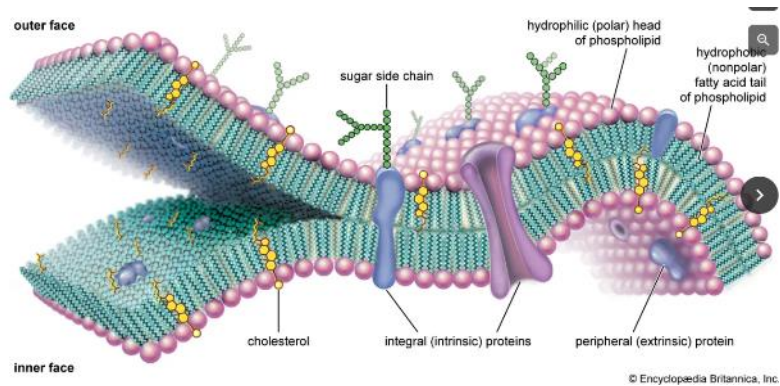


There is an ongoing translation of indications within surgical HCC

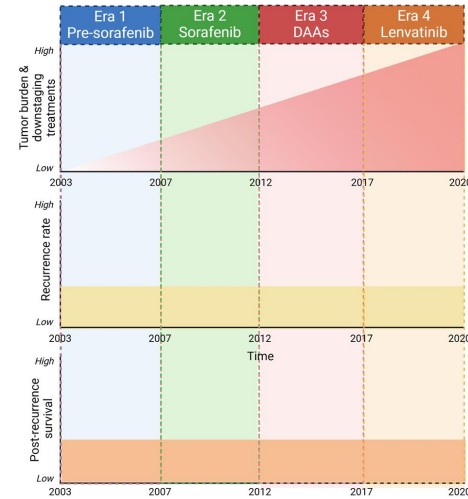
There is an ongoing translation to transplant from non surgical HCC



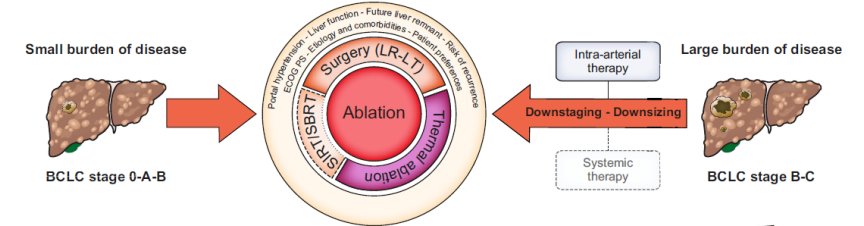
In conclusion,



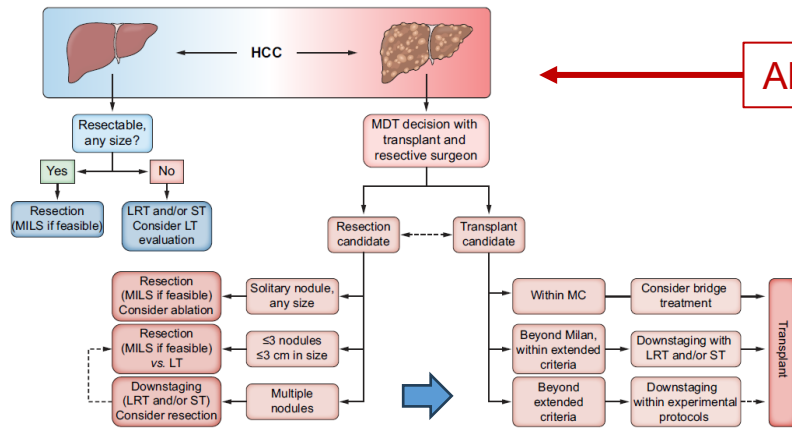
Barriers are essential to life



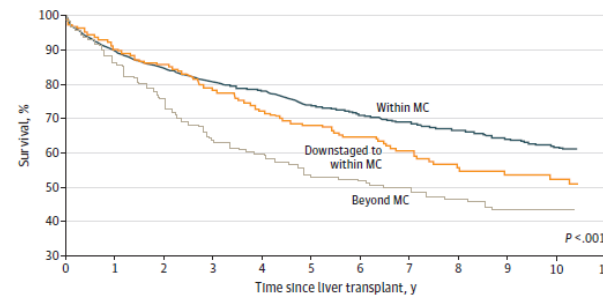
Tumor burden is a barrier that can be managed with non-transplant means



We are entering an era of Translation in outcome predictions and decision-making

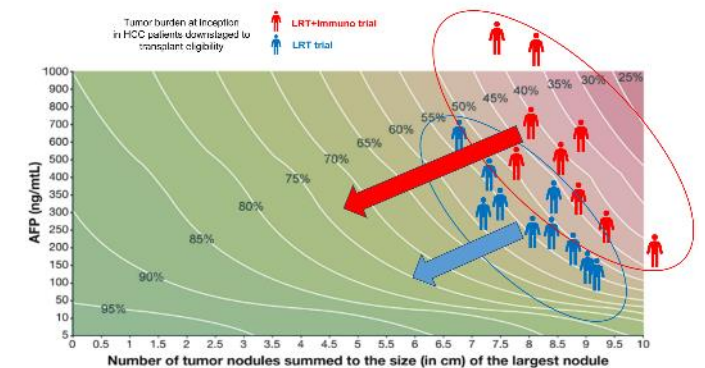


All under restrictive criteria



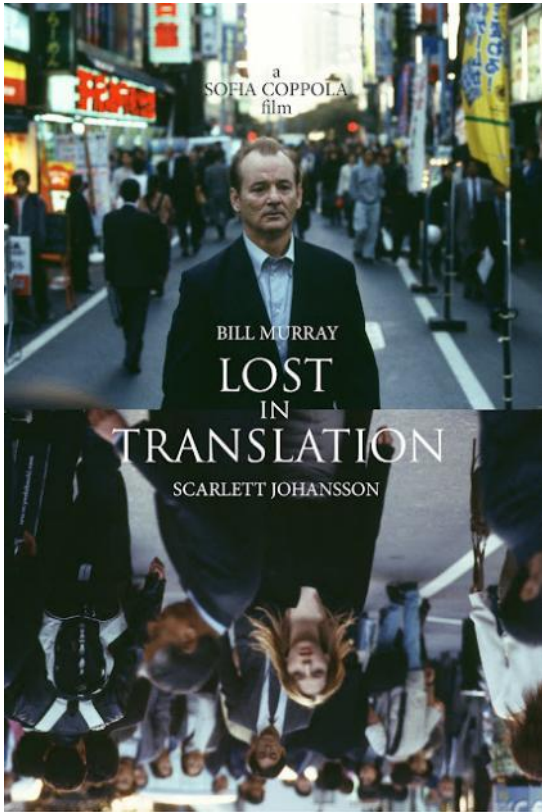
There is an ongoing translation of indications within surgical HCC

There is an ongoing translation to transplant from non surgical HCC



Systemic therapies are producing the most significant LT criteria expansion to date



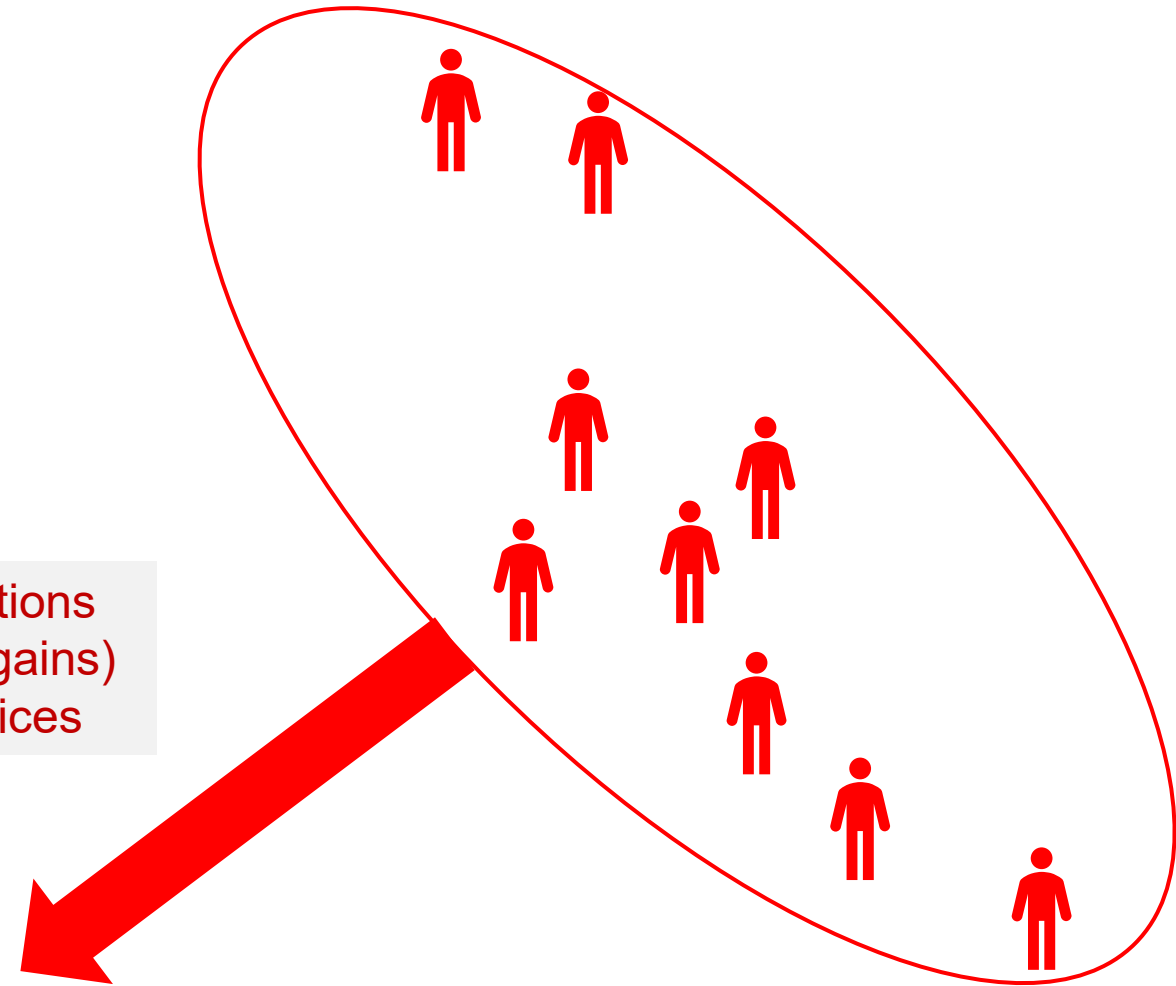


More than two decades later,  
this is still one of the best film.  
An exquisite dramedy that stays with you  
long after the credits roll.

*Urban Cinefile*

Positive transformations  
during translations (gains)  
depend on our choices

**Thank you very much for  
your attention**



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[vincenzo.mazzaferro@unimi.it](mailto:vincenzo.mazzaferro@unimi.it)